ESTIMATION OF UREA AND CREATININE IN VAGINAL FLUID IN PRETERM PRE-LABOUR RUPTURES OF MEMBRANES

A THESIS SUBMITTED TO

BABA FARID UNIVERSITY OF

HEALTH SCIENCES, FARIDKOT (PUNJAB)

IN THE PARTIAL FULFILLMENT

FOR THE AWARD OF DEGREE OF

DOCTOR OF MEDICINE

IN

Obstetrics & Gynaecology

MAY 2023

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DECLARATION BY THE CANDIDATE

I hereby declare that the thesis entitled **"ESTIMATION OF UREA AND CREATININE IN VAGINAL FLUID IN PRETERM PRE-LABOUR RUPTURE OF MEMBRANES**" submitted towards partial fulfillment of the requirements for the award of **MD in Obstetrics & Gynaecology** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Sunil K. Juneja**, Professor, Department of Obstetrics & Gynaecology, **Dr. Navjot Kaur Bajwa**, Professor, Department of Biochemistry and **Dr. Shweta Gupta**, Professor Department of Obstetrics & Gynaecology No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

My Parents

Friends

And

Teachers

ACKNOWLEDGEMENT

At the onset of every major task, difficulties are seen insurmountable. But gradually as we tread the chosen path with honesty and perseverance, God helps at every step. I am grateful to God Almighty with whose blessings this project could be successfully completed.

Words won't suffice to express my indebtedness and a deep sense of gratitude for my respected teacher and supervisor ***Dr. Sunil Kumar Juneja*** *Professor, Department of Obstetrics and Gynaecology, Dayanand Medical College, Ludhiana. His guidance helped me the entire time from the genesis to the culmination of this study. His unabated inspiration, keen critical acumen, and timely guidance have always helped and I could not imagine having a better advisor and mentor. I take great pride in expressing my gratitude to him.*

I am very thankful to my Co-supervisor ***Dr. Navjot Bajwa****, Professor Department of biochemistry, Dayanand Medical College, Ludhiana for their indelible help and fervent interest at all stages that helped me a long way in the completion of this project.*

I would also like to say special thanks to my Co-supervisor ***Dr. Shweta Gupta*** *Professor Department of Obstetrics and Gynaecology, Dayanand Medical College, Ludhiana for constant support, encouragement, enlightening me throughout my project. This accomplishment would not have been possible without her help.*

I would also like to say special thanks to my Head of Department. ***Dr. Ashima Taneja****, Professor, and Head, Department of Obstetrics and Gynaecology, Dayanand Medical College, Ludhiana for constant support, encouragement, enlightening me throughout my project. This accomplishment would not have been possible without her help.*

My sincere thanks to ***Dr. Suman Puri, Dr. Pooja Tandon, Dr Kanupriya Jain, Dr. Monika Narang*** *for their constant support and immense guidance. I consider it my privilege and good luck to have an opportunity to work under such teachers of their eminence.*

No words are enough to thank my mother ***Mrs Kirpal kaur*** *and father* ***Mr Sita Ram*** *and my brother* ***Sunil Kumar Ladher*** *and sister* ***Suman***

Ladher *whose care, affection timely help and encouragement have been constant source of inspiration throughout the study.*

I would also like to say special thank to my senior and mentor ***Dr.Riddhima Gupta*** *whose constant guidance and suggestions have helped me throughout my research. This accomplishment would not have been possible without her help.*

Words are woefully inadequate to express my sense of gratitude to my seniors ***Dr. Reetika , Dr. Manpreet, Dr. Muskan, Dr Gagandeep, Dr Barbie , Dr Pavneet, Dr Gaurav , Dr Harmeet my colleagues Dr. Amadeep ,Dr Mehak ,Dr Rashim*** *for their support and my juniors especially* ***Dr. Janvi, Dr. Baljinder, Dr. Romi,*** *being so cooperative and helpful* ***Mrs. Renu*** *for being caring and helpful.*

A special thanks to my best friend ***Dr Jasmeet kaur*** *for her indebted support and kept me motivated.*

A special thanks to ***Mrs. Renu*** *for her indebted support.*

I would like to extend my thanks to ***Mrs. Namita, Mrs. Niharika Kochar*** *and other Research and development center staff for rendering their kind services helpful in the successful completion of the thesis.*

I bow my head in sincerely acknowledging all my patients who kindly consented to become the subject of the thesis. Without their cooperation, this study would not have been the light of the day.

Dr Heena.

LIST OF ABBREVIATIONS

ACOG	American college of obstetrics and gynaecology
AFI	Amniotic fluid index
AFP	Alpha-fetoprotein
ANOVA	Analysis of Variance
Beta HCG	Beta- human chorionic gonadotropin
BMI	Body mass index
CI	Confidence interval
DEFB1	Defensin beta 1
EGF	Epidermal growth factor
ESR-2	Estrogen receptor 2
FWB	Fetal well being
HCG	Human chorionic gonadotropin
HPL	Human placental lactogen
IGFP-1	Insulin growth factor binding protein -1
MD	Mean deviation
ml	Mili litres
MMP	Matrix metalloproteinases
MSAF	Meconium-stained amniotic fluid
NFkB	Nuclear factor kappa B
NPV	Negative predictive value
PAMG-1	Placental alpha-microglobulin -1
PGE2	Prostaglandin E2

PPROM	Preterm pre-labour rupture of membranes
PPV	Positive predictive value
PROM	Prelabour rupture of membranes
P/S	Per speculum
p-value	Probability value
ROC	Receiver operater curve
SD	Standard deviation
Std	Standard
STAT-1	Signal Transducer and Activate of Transcription
TNF alpha	Tumour necrosis factor alpha
TTNB	Transient Tachypnea of newborn
USG	Ultrasonography
UTI	Urinary tract infection

ABSTRACT

Introduction:- PPROM is rupture of membranes before 37 weeks period of gestation and before the onset of labour. Accurate PPROM diagnosis is essential for timely patient management.

Aim of Study: To evaluate urea and creatinine values in vaginal fluid as a markers of PPROM and to determine the diagnostic cutoff values of vaginal fluid urea and creatinine levels in PPROM and to give suitable recommendations based on the study findings

Materials & Methods: This was a prospective case control study. Women having gestational age between 28 to 36 weeks 6 days were divided into three equal groups: Group A (cases) 50 pregnant women with history of leaking per vagina and confirmed leak on P/S examination Group B (suspected)50 pregnant women with history of leaking but not confirmed on P/S examination. Group C (control) 50 pregnant women with no leaking per vaginum were recruited. Data analysis was done by ANOVA and chi square test for vaginal fluid urea and creatinine.

Results: The mean vaginal fluid urea levels in group A,B and C were 9.16 +/- 6.01 mg/dl, 2.06+/- 0.82 mg/dl and 0.75+/- 0.48 mg/dl and mean creatinine values 0.52+/-0.47 mg/dl ; 0.13+/-0.08 mg/dl and 0.1+/-0.23 mg/dl respectively where the difference was statistically significant ($p<0.001$). The optimum cut off value for vaginal fluid urea in Group A and B was ≥2.5 mg/dl and ≥1.5 with sensitivity, specificity 98%, 100% and 82% ,96% respectively and cut off values for creatinine was≥ 0.2mg/dl and is ≥0.1 with sensitivity, specificity 88% ,80% and 46% ,60% respectively.

Conclusion: In our study we conclude that urea and creatinine in the vaginal fluid are reliable markers for the diagnosis of PPROM. Urea is a better predictor with high sensitivity and specificity. Measurement of these markers in vaginal fluid is easy, cost effective and can be performed without much technical assistance. Thus these markes can be used for improving the diagnosis of PPROM so as to make rational and safe use of available therapeutic strategies.

Keywords: Preterm prelabour Rupture of Membranes (PPROM); Urea; Creatinine; Vaginal fluid.

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KEY TO MASTER CHART

+	POSITIVE
-	NEGATIVE
P	PRESENT
S	SUSPECT
A	ABSENT
W	WET
D	DRY

INTRODUCTION

Pre-labour rupture of membranes (PROM) is defined as the rupture of membranes before the onset of labour.[1]Earlier it was called the "premature rupture of membranes" which was sometimes misinterpreted as "fetal prematurity" thus the use of both "preterm" and "premature" to define the condition was confusing. It has been recently modified to "pre-labour rupture of membranes", the abbreviation (PROM) as well as the definition of the condition has not been changed and are satisfactorily consistent worldwide. The new term is more accurate and acceptable. It should be widely used instead of the old term. Thus the use of the new term is highly recommended as compared to the old one.[1,2,3]

Pre-labour rupture of membranes is classified according to the gestational age at which it occurs into:-

- TERM PROM
- PRETERM PROM
- PREVIABLE PROM

TERM PRE-LABOUR RUPTURE OF MEMBRANES (PROM):- Rupture of the membranes at or more than 37 weeks period of gestation before the onset of labour.[,3]

PRETERM PRE-LABOUR RUPTURE OF MEMBRANES (PPROM):- Rupture of membranes before 37 weeks period of gestation and before the onset of labour.[4]

PRE-VIABLE PRE-LABOR RUPTURES OF MEMBRANES (**PRE-VIABLE PROM**):- is defined by ACOG as a rupture of the membranes occurring before the period of viability [as early as 23 0/7 weeks gestation]. [5] This category differs from the other two categories of PROM, as counseling and treatment differ significantly. Although this definition of

pre-viable PROM is widely accepted, the definition of viability has changed over time and varies widely between low and high-resource countries.

EPIDEMIOLOGY-:The incidence of term prelabour rupture is about 8% [8]and preterm prelabour rupture is 3% worldwide.[2,9,10]Spontaneous onset of labor in term PROM is about 86% and in preterm births, PROM is about 30-40%.[11-13] Typically, labor begins within 12 to 24 hours of the rupture of the membrane. [1]

RISK FACTORS FOR PRETERM PRE-LABOUR RUPTURE OF MEMBRANES:-

Infection:- A significant proportion of PPROM cases are caused by infections. It is estimated that 25-40% of preterm births are due to intrauterine infections. They activate the innate immune system. Microorganisms cause the release of inflammatory cytokines such as interleukins and TNF-alpha. These cytokines stimulate the production of prostaglandins such as prostaglandin E and matrix-degrading enzymes. Degradation of the extracellular matrix in fetal membranes caused by matrix-degrading enzymes leads to preterm prelabour rupture of the membranes.[13]

PPROM in a previous pregnancy:- The risk of recurrence is three times higher in women with a previous history of PPROM. It has been shown that the causes of previous preterm birth can also recur in the subsequent pregnancy [14]

Antepartum Vaginal Bleeding:- Light or heavy per vaginum bleeding, placental abruption increases the risk for intra-amniotic infection and inflammation. The infection leads to increased production of tissue factor in the decidua, which results in the formation of thrombin. This thrombin causes activation of matrix metalloproteinases (MMPs), leading to degradation of the extracellular matrix of fetal membranes and recruitment of neutrophils, which in turn increases local cytokine activity. Thus, MMP-

mediated collagenase activity and cytokine-mediated increase in cellular apoptosis lead to the weakening of membranes, resulting in PPROM.[15-20]

Life Style Factors:- cigarette smoking causes nutritional deficiencies { vitamin C and B-carotene}and reactive oxygen species generated by smoking may contribute to the development of PPROM.[21] Illegal drugs (cocaine), low body mass index (BMI <19.8 kg/m2), low socio-economic status, and deficiency of copper and ascorbic acid in the diet[23-24]. Although each of these risk factors is associated with preterm birth, PPROM, the condition occurs frequently without any recognized risk factors or obvious cause. **Anemia** leads to alterations in the modulation of immune cells such as T and B cells. As a result, their proliferation, phagocytic and bactericidal activity may be reduced. The presence of infection increases the chances of PPROM.[25-28]

Genetic Factors:- Alterations in genes responsible for inflammation and collagen formation may be responsible for PPROM. Example STAT1, ESR2andNFκB complex, DEFB1 nonsense variant, etc. [29;30]

Other factors:-Chronic steroid therapy:- Cortisol is endogenously elevated in the mother and fetus during labor, resulting in the weakening of fetal membranes, which is considered physiologic because rupture of the membranes during labor is a natural part of the birth process. However, exogenous glucocorticoid therapy may have adverse effects on fetal membranes leading to PPROM. Glucocorticoid therapy suppresses the immune system and increases the risk of infection. Glucocorticoids directly reduce various extracellular matrix proteins of both epithelial and mesenchymal cells of the amnion.[31]**Collagen vascular disease** (e.g., Ehlers-Danlos syndrome, systemic lupus erythematosus):- impaired collagen synthesis - thinning of membranes.

Direct abdominal trauma, uterine manipulation, uterine massage by traditional healers, penetrating abdominal trauma.

Periodontal disease:- Gum inflammation is a chronic anaerobic inflammation that affects around 50% of pregnant women. Failed treatment significantly alters preterm birth rates.[32]

Abnormalities of the uterus:- (e.g. uterine septum) Due to abnormal development there reduced cervical connective tissue and increased muscle composition that are insufficient to withstand the increased and asymmetrical uterine pressure after pregnancy; hence, preterm delivery, abnormal foetal positioning, and other risks were significantly increased.[33]

Earlier cervical conization:- Prior cervical conization may impair the antimicrobial defense-mechanisms in the cervix, which could facilitate ascending microbial colonization. This may lead to a release of prostaglandins and proteolytic enzymes and subsequently preterm labor and rupture of the membranes.[34]

Multiple pregnancies:- (preterm delivery PROM complicates 7-10% of twin pregnancies) Uterine overdistension.[35] excessive uterine stretch also leads to early activation of the placental-fetal endocrine cascade.

Polyhydramnios:-(increased mechanical stretching of the fetal membranes can also lead to loss of integrity and thus rupture of the membranes far from term)

PATHOPHYSIOLOGY:-Fetal membranes are extraembryonic tissues that surround the fetus and form a maternal-fetal interface. They are multilayered tissues consisting of two main layers:Amnion and Chorion.

Collagen is the major structural component of fetal membranes and provides tensile strength to membranes, Maintenance of balance between synthesis and degradation of collagens in fetal membranes play important role in the integrity of membranes throughout pregnancy.

The weakening of fetal membranes is a natural process that normally occurs at the time of birth. If this process occurs before 37 weeks

(prematurity), it can lead to fetal or maternal complications. The natural weakening of fetal membranes may be due to one or a combination of the following:- Cell death:- when cells undergo programmed cell death, they release apoptotic biochemical substances that are detected in higher concentrations in PPROM. The insufficient buildup of collagen:- collagen is a molecule that gives strength to fetal membranes as well as other parts of the human body, such as the skin. In PPROM, the proteins that bind and cross-link collagen to increase its tensile strength are altered. Collagen degradation: collagen is degraded by enzymes called matrix metalloproteinases (MMPs), which are present in elevated concentrations in PPROM. This degradation leads to the production of prostaglandins, which stimulate uterine contractions and cervical maturation. [36-39]Infection and inflammation may be one of the factors responsible for preterm prelabour rupture of membranes. Bacterial infection leads to the release of chemicals [cytokines] that subsequently weaken fetal membranes.[40,41]

COMPLICATIONS OF PRETERM PRE-LABOUR RUPTURE OF MEMBRANES:-

MATERNAL COMPLICATION:-

1. **Chorioamnionitis:-** it is a major concern with membrane rupture. Out of all cases of PPROM 25% develop chorioamnionitis.[42] The risk of intrauterine infection increases with the duration of membrane rupture and with declining gestational age, due to decreased antibacterial activity of amniotic fluid remote from term. Fetal and neonatal morbidity are substantively increased with chorioamnionitis due to high incidence of sepsis, respiratory distress syndrome., Early onset seizures, intraventricular hemorrhage, periventricular leucomalacia.

2. **Placental separation and abruption:-** Placental abruption affect 4-12% of pregnancies with PPROM. [43]

3. **Postpartum endometritis:-** Postpartum endometritis is a frequent maternal complication in women with PPROM, particularly if the patient develops chorioamnoinitis.

4. **Risk of operative delivery:-** Caesarean delivery rates significantly increase in PPROM, secondary to obstetric complications such as fetal malpresentation, non-reassuring fetal heart patterns, cord compression, and placental abruption

NEONATAL COMPLICATIONS:-

Respiratory distress syndrome

Transient tachypnea of the newborn (TTNB)

Congenital pneumonia, Pulmonary hypoplasia

Neonatal infection.

Necrotising enterocolitis

Neurological disorders

DIAGNOSIS

A patient with symptoms suggestive of PPROM should be examined promptly. The examination includes a history of the patient and an examination of the cervix to assess the gross accumulation of amniotic fluid. A thorough history, clinical examination, and special tests are the most important requirements for the diagnosis of preterm prelabour rupture of membranes.

The three conventional findings that are considered the gold standard are obtained by the clinician for the diagnosis of preterm prelabour rupture of membranes. **1)** Observation of clear amniotic fluid flow or fluid collection at the posterior fornix with a sterile speculum. **2)** Observation of transition from yellow to blue with pH indicator paper due to basic amniotic fluid flow

(nitrazine test) **3)** Detection of palm leaf patterns in dried amniotic fluid by microscopic method (fern test). [44]

However, the above conventional methods also have some limitations. Patient-reported history, which is reliable in 10% to 50% of cases in speculum testing for amniotic fluid leakage, has been associated with 12% to 30% false-negative results [45]

Nitrazine testing has been associated with false-positive or negative results due to contamination from urine, blood or meconium, antibiotics, and vaginal and cervical infections. [46,47,48]

The fern test has also been associated with 13-30% false negative and 5-30% false positive results. The sensitivity of this test ranges from 51% to 98% and the specificity ranges from 70% to 78%. [45]

Ultrasound is also not a reliable test for the evaluation of rupture of the membranes because it cannot distinguish PPROM from other causes of oligohydramnios. Thus diagnosis by conventional methods generally becomes difficult when more than one hour has elapsed after amniotic fluid leakage [35].

Avoiding adverse outcomes without diagnosis or unnecessary interventions due to misdiagnosis may require the use of invasive methods.

In the Amnio dye test (also called tampon test), indigo carmine is injected into the amniotic cavity by Amnio infusion. The tampon in the vagina is evaluated after 20-30 minutes. Although described by some authors as the gold standard diagnostic method, this invasive test carries risks such as placental abruption, iatrogenic PROM, infection, and pregnancy loss [49,50]

The Amnisure membrane rupture test is another new test that is simple, rapid, non invasive and has high sensitivity and specificity. However, the Amnisure test is not available in many centers and is also expensive.

Other diagnostic modalities and biochemical tests for PPROM have been described, such as measurement of alpha-fetoprotein (AFP), insulin growth factor binding protein-1 (IGFBP-1),fetal fibronectin human chorionic gonadotropin (HCG),prolactin and lactate.[51-54]

The reason for evaluating these markers is due to their high concentrations in amniotic fluid compared to normal vaginal secretions. These tests are based on the presence of one or more biochemical markers in vaginal secretions during premature rupture of membranes and are not detectable in women with intact membranes. However, these tests are complex and too expensive, so they are not widely used for routine evaluation of PPROM, despite the improved diagnostic potential of these biochemical markers.[52-54]

False-positive diagnosis of Preterm prelabour rupture of membranes by conventional methods may lead to inappropriate management or unnecessary obstetric interventions. Failure to diagnose Preterm prelabour rupture of membranes in time can lead to maternal and fetal complications.

No optimal screening test is present currently for PPROM in low-risk asymptomatic patients. Accurate PPROM diagnosis is essential for proper patient management. Traditional approaches to the diagnosis of rupture of fetal membranes are now powered by scientific progress. Biomarkers have a major role to play in this area. The search for an accurate test is still going on. An ideal test should be rapid, accurate, noninvasive, inexpensive, easily applicable, and available and should be present in cervicovaginal secretions when rupture of membranes has occurred, whereas it should be absent in case of intact membranes.[54-56]

Nowadays, the emphasis is on the measurement of urea and creatinine in vaginal fluid for the diagnosis of Preterm pre-labour rupture of membranes. This is based on the hypothesis that the prime component of amniotic fluid in the second half of pregnancy is fetal urine. The fetus starts excreting urine into the amniotic fluid between 8th to 11th week of gestation. This test is very cheap, and cost-effective in comparison to other biomarkers.[56] There is no requirement for additional equipment and reagent for the collection of samples and testing. Therefore the introduction of this method is both feasible and practical in routine workups in both developed and developing areas.

Thus the present study is proposed to evaluate the reliability of vaginal washing fluid urea and creatinine for the diagnosis of Preterm prelabour rupture of membranes and to establish the cutoff value for urea and creatinine in vaginal washing fluid.

AIMS AND OBJECTIVES

AIM:- To evaluate urea and creatinine values in vaginal fluid as a markers of preterm pre-labour rupture of membranes.

OBJECTIVES:- To determine the diagnostic cutoff values of vaginal fluid urea and creatinine levels in preterm pre-labour ruture of membranes and to give suitable recommendations based on the study findings.

REVIEW OF LITRATURE

The amniotic fluid surrounding the embryo and fetus during development serves a variety of purposes and provides a safe environment for the fetus during pregnancy and birth.

ROLE OF AMNIOTIC FLUID:-

The amniotic fluid serves several functions for fetal growth and labor.

The role of amniotic fluid in fetal growth:

- Enables fetal breathing, maintains amniotic fluid pressure, and thus reduces the loss of lung fluid necessary for lung development. [57,58]
- Amniotic fluid has bacteriostatic and bactericidal properties, helping to prevent infections [59]
- It creates a physical space for fetal movement, which contributes to normal fetal musculoskeletal development. It also helps in stretching the limbs and prevents contractures. It protects the fetus from trauma.
- The swallowing of amniotic fluid by the fetus in the womb helps in the development of the gastrointestinal tract. Because amniotic fluid contains many trophic factors[60,61]
- It regulates the temperature of the fetal body. [62]
- Amniotic fluid has a minimal nutritional function.
- It contains many trophic factors such as epidermal growth factor (EGF) and EGF-like growth factors such as transforming growth factor-β. [61,62]

Role of amniotic fluid during labour:

- Acts as a hydrostatic wedge helping in the dilatation of the cervix.
- It helps in the even distribution of the pressure of uterine contraction over the fetus.
- Prevents umbilical cord compression

DEVELOPMENT OF AMNIOTIC FLUID:-

The formation of amniotic fluid is not well understood to date. It has both maternal and fetal origins. Amniotic fluid is approximately 98 percent water [63]. In early pregnancy, amniotic fluid is an ultrafiltrate of maternal plasma.

In the second trimester, it consists mainly of extracellular fluid that diffuses through the fetal skin because it is only four layers thick, reflecting the composition of fetal plasma and known as the "intra-membranous pathway."

There are several pathways for the formation of amniotic fluid (fetal urine, early transfer through fetal skin, and lung fluid production), and for its removal (swallowing, transmembranous, and intramembranous uptake). After 20 weeks of gestation, keratinization of the fetal skin prevents this diffusion and the amniotic fluid consists mainly of fetal urine[64,65,66]

The fetal kidneys and lungs are two major sources of amniotic fluid in the second half of pregnancy. Urine has been observed in the fetal bladder as early as week 11 with transabdominal ultrasound and week 9 with transvaginal ultrasound. [67,68,69]. By week 18, they produce 7 to 14 ml of urine per day. The amounts of urea, creatinine, and uric acid are higher in fetal urine than in fetal plasma. Confirmation of the role of the kidneys in amniotic fluid production is based in part on the finding that in the third trimester, the concentrations of sodium and chloride in fetal amniotic fluid and urine decrease, while the concentrations of urea and creatinine increase in both fluids [70]. In addition to the fetal kidneys, the lungs also

contribute to the total volume of amniotic fluid. Although the exact amount of amniotic fluid secreted by the lungs is unknown, it is estimated to be in the range of 60 to 100 ml/kg/day of fetal weight at birth. [71,72]

Desquamated fetal cells, vernix, lanugo, steroidal and nonsteroidal hormones (corticosteroids, progesterone, estriol, HCG human chorionic gonadotropin, HPL human placental lactogen), carbohydrates, electrolytes, lecithin, and phospholipids also form the components of amniotic fluid. Amniotic fluid also includes fetal and various secretions. Because these are hypotonic, the osmolality of amniotic fluid decreases as pregnancy progresses. [73]

During the first half of pregnancy, amniotic fluid is derived from fetal and possibly maternal compartments. Water and solutes can freely permeate the fetal skin and also diffuse through the amnion and chorion. In the second trimester, the fetal skin becomes keratinized and thus impermeable to further diffusion. Measurement of urea and creatinine levels in vaginal fluid for the diagnosis of preterm prelabour rupture of the membranes is based on the concept that fetal urine is the main component of amniotic fluid during this period.

TABLE:-1 PRODUCTION OF AMNIOTIC FLUID AT DIFFERENT GESTATION:- [65,66]

No.	**GESTATION AGE**	**SOURCE OF AMNIOTC FLUID**
1	UPTO 20WKS	FETAL AND MATERNAL PLASMA
2	AFTER 20WKS	FETAL URINE

Table:-2 CHANGE IN VOLUME OF AMNIOTIC FLUID AT DIFFERENT GESTATION[75-77]

No.	Weeks of gestation	volume
1	10	10-20ml
2	12	60ml
3	16	175ml
4	20	400ml
5	34-38	1000ml
6	40	800ml
7	43	250ml

This reduction after 38 weeks may reflect a shift of cardiac output away from the kidneys as a result of a relative uteroplacental insufficiency.

Table:- 3. RATE OF CHANGE AMNIOTIC FLUID VOLUME:- [75-77]

No.	weeks of gestation	Rate of change per week
1	8	Increase 10 ml/week
2	13	Increase 25ml/week
3	21	Increase 60ml/week
4	33	Zero
5	>33	Decline by 8% /week

AMNIOTIC FLUID REGULATION:-

The most important source of elimination is fetal swallowing, which is observed as early as 16 weeks. [72] In late pregnancy, the approximate daily amount of amniotic fluid reabsorbed by swallowing is 500-1000 mL. [74]

Another means of amniotic fluid reabsorption is intra-membranous fluid transfer across and into fetal vessels on the placental surface. This is due to the hypotonicity of fetal urine and thus amniotic fluid accounts for approximately 400 ml of volume reabsorption per day. [73]

Another pathway for amniotic fluid volume regulation is transmembranous flow and flow through fetal skin, which accounts for a small portion of amniotic fluid reabsorption in late pregnancy.

Table 4:- Regulation of amniotic fluid in pregnanacy.[72-74]

PATHWAY	**EFFECT ON VOLUME**	**APPROXIMATE DAILY VOLUME (ml/day)**
Fetal urination	Production	1000
Fetal lung fluid secretion	production	350
Fetal swallowing	Reabsoption	750
Intra-membranous flow across the fetal vessels on the placental surface	Reabsorption	400
Transmembranous flow across amniotic membrane	Reabsoption	minimal

UREA AND CREATININE AS A COMPONENT OF AMNIOTIC FLUID:-

Creatinine is a breakdown product of creatinine phosphate (in the muscle), it is usually produced at a fairly constant rate by the body depending on the muscle mass. Creatinine is usually used to evaluate kidney function. The normal creatinine clearance test value in females is (100-130ml/min) & (110-150ml/min) in males [78].

Urea is the major nitrogenous end product of amino acid & protein catabolism. It is produced by the liver and distributed all over the intracellular and extracellular fluids. A normal amniotic fluid volume was first considered the only indicator of fetal kidney development, but the concentration & origin of many biochemical substances begin to be investigated later [79].

In pregnant women in the first half of pregnancy, the mean creatinine concentration in amniotic fluid is 0.6 mg/dl, which is similar to that in maternal serum [80,81]. In amniotic fluid, a gradual increase in creatinine concentration is observed between 20 and 32 weeks of gestation, which rises even more rapidly to reach a value as high as two to four times that of maternal serum [80,81] Creatinine and urea analysis in the amniotic fluid also gives an approximation of renal function maturing throughout pregnancy. Creatinine values in the amniotic fluid that best represent fetal maturity are 1.5 to 2.0 mg/dl. A creatinine concentration of 1.75 mg/dl or more correlates significantly with a gestational age of 37 weeks or more [78,79]. Many studies have proved this in their research that a rising level of urea and creatinine in amniotic fluid is found in preeclampsia. Thus urea and creatinine in amniotic fluid plays an important role in the evaluation of many obstetric conditions.

Preterm prelabour rupture of the membranes is the spontaneous rupture of membranes before the onset of labour is a common obstetric condition that causes increased maternal and perinatal morbidity and mortality.

Therefore the correct and timely diagnosis of rupture of membranes is essential for optimizing, pregnancy outcomes, and management is based on accurate diagnosis and cost-effectiveness, the noninvasive diagnostic gold standard test has yet to become available.

Table 5:- Difference in maternal urine and amniotic fluid creatinine and urea levels [81,82]

Sample	Creatinine mg/dL	Urea mg/dL
Amniotic fluid	<3.5	<30
Maternal urine	>10	>300

Measurement of urea and creatinine levels in vaginal washing fluid to diagnose a preterm prelabour rupture of the membranes is based on the concept that fetal urine is the major component of amniotic fluid in the second half of pregnancy. Therefore, the present study aims to evaluate the reliability of urea and creatinine levels in amniotic fluid for the diagnosis of the preterm prelabour rupture of membranes and to determine the cutoff value for urea and creatinine in amniotic fluid.

The reliability of conventional tests does not match the patient's history of leakage, so the search for simple, rapid, accessible, and noninvasive diagnostic methods to detect the rupture of membranes remains in demand. Since no additional equipment and reagents are required, the introduction of this method into routine use is feasible and practical. This study examines the diagnostic accuracy of vaginal fluid urea and creatinine, which are readily available in low-resource communities to detect early preterm prelabour rupture of membranes

Kafali et al [2007] were the first to use urea for the diagnosis of preterm prelabour rupture of membranes. In their study, sensitivity, specificity, negative predictive value, and positive predictive value were 100% for the

detection of preterm prelabour rupture of membranes by evaluation of vaginal fluid urea and creatinine concentration with cut-off values of 12 and 0.6mg/dl respectively [83].

Mohamed et al. study in which 298 women were included and divided into 3 groups (122 with confirmed ruptured membranes, 96 with suspected but not confirmed ruptured membranes & 80 with intact membranes), found 100% sensitivity, specificity, negative predictive value and positive predictive value of evaluation with cut off of urea 13.2 mg/dl and creatinine 0.31mg/dl in detecting Preterm prelabour rupture of membranes [84].

Kariman et al. [2013] also studied 2 groups to compare vaginal fluid urea and creatinine in confirmed cases and normal controls. They found the mean level of vaginal fluid urea and creatinine in the Preterm prelabour rupture of membranes group to be significantly higher than in the control group.[45]

Osman et al. [2014] studied 3 groups, a prospective study performed on 150 pregnant women in their third trimester (28 - 40 weeks) and compared AFI and vaginal fluid urea, creatinine, and β-hCG. They showed a statistically significant difference among all groups regarding AFI, urea, creatinine, and β-hCG levels. They found sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of urea and creatinine were all 100% with a cut-off value of > 0.41 mg/dl and > 0.23 mg/dl. They concluded urea and creatinine in vaginal washings can be accurately used in diagnosing suspected preterm prelabour rupture of membranes and are more accurate than β-hCG[85].

Tigga et al. [2015] studied 2 groups, and compared vaginal fluid alpha-fetoprotein, prolactin creatinine, and β-hCG. They found that all four markers were significantly higher in the patients with preterm prelabour rupture of membranes in comparison to those without preterm prelabour rupture of membranes. They found sensitivity, specificity, positive

predictive value, negative predictive value, and efficiency of creatinine were 100%, 92%, 92.59%, 100%, and 96% efficiency with a cut-off value of 0.1641 mg/dl and Creatinine was reported to be a simple, cheap, reliable and easily available method for diagnosing PROM [55]

Ghasemi et al. [2016] studied in 2 groups, 80 confirmed PROM patients and 80 controls, and compared vaginal fluid prolactin, β-hCG, urea, and creatinine. They also showed that all four markers were significantly higher in the patients with Preterm prelabour rupture of membranes in comparison to those without PPROM ($p < 0.001$). An optimal cutoff level of 3.5 mg/dl for urea and 0.25 mg/dl for creatinine was seen in their study. The sensitivity, specificity, and positive and negative predictive values to diagnose PROM were calculated and found to be 79.7%, 82.5%, 81.8%, and 80.4% for urea and 74.6%, 85%, 83%, and 77.2% for creatinine. They reported less diagnostic value of urea and creatinine for detecting preterm prelabour rupture of membranes because of the difference in laboratory method analysis and cut-off points [56]

Gezer et al. [2017] conducted a study with an optimal cutoff level of 6.7 mg/dl for urea and 0.12 mg/dl for creatinine in vaginal fluid. They finally came up with a suggestion that urea levels > 6.7 mg/dl and creatinine levels> 0.12 mg/dl in vaginal fluid, to diagnose PPROM in approximately 88% and 89% of women respectively if seen between 24 and 37 weeks. They also hinted that in patients with shorter delivery intervals, raised vaginal urea and creatinine levels may suggest a large defect in the amniotic membrane or increased production by the fetus. [86]

Zanjani et al. [2012] studied the reliability of vaginal fluid creatinine for the diagnosis of premature rupture of membranes. The creatinine level was significantly higher in the confirmed group than in the other two groups ($P < 0.0010$). They found 96.7% sensitivity, 100% specificity, 100% positive predictive value, and 96.8% Negative Predictive value with an optimal cutoff value of 0.5mg/dl. They concluded that it is a valid and simple test,

especially considering that it costs much less than hospitalization or other tests [87].

Gada et al in the year 2018 studied the reliability of vaginal fluid urea and creatinine levels for the diagnosis of PPROM. This study showed that there was a significant difference in the levels of creatinine and urea in the studied groups. The creatinine level was 0.64, 0.28, and 0.14 in confirmed, suspected, and controls respectively. The urea levels were 29.67, 5.51, and 1.68mg/dl in confirmed, suspected, and controls respectively. These findings are similar to that obtained in our study where the highest levels of urea and creatinine were seen in the confirmed or Group - 1 cases. Levels of both urea and creatinine were almost insignificant in the control group.[88]

Sabee et al studied 96 women and divided them into 3 groups as in our study. They found vaginal fluid urea and creatinine level were significantly higher in women of the confirmed group compared to the suspected and control group. [89] These findings are exactly similar to the results obtained in your study.

Kedar, Kashma, et al [2018] in their study of found creatinine at a threshold value of 0.668 mg/dL had a sensitivity, specificity, PPV, NPV, and accuracy of 100%, 91.25%, 91.95%, 100%, and 95.62% respectively. In the diagnosis of PROM for a threshold value of 9.906 mg/dL for urea, the sensitivity, specificity, PPV, NPV, and accuracy were 100%, 92.5%, 93.02%, 100%, and 96.25% respectively in the detection of PROM.[90]

Alao, A.I., Afolabi et al [2022] in their study on vaginal fluid urea and creatinine, an untapped diagnostic tool for premature rupture of membranes has found that vaginal fluid urea and creatinine are very effective tests in the diagnosis of PROM. It is a cheaper and more readily available alternative to the Amnisure test. It is especially useful in our environment, especially in cases of equivocal PROM, as a cost-effective

means to confirm the diagnosis. Vaginal fluid urea and creatinine had sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV), respectively, of 94%, 82%, 93.18%, and 83.93%, and 98%, 90%, 97.82%, and 90.74%. The cutoff values for vaginal fluid urea and creatinine were 1.25 mg/dl and 0.23 mg/dl, respectively.[91]

A study was conducted by Li Hy et al determine AFP and creatinine measurements in the detection of PROM. In that study 10 control patients and 10 confirmed PROM cases were included and the results showed that the sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of creatinine were 90%, 100%, 100%, 90.9%, They found that creatinine in vaginal fluid washings is a useful marker for PROM diagnosis. It was less expensive and easier to measure than hCG and AFP and appeared to be more accurate than hCG. [92]

In a study by Gurbuz et al, the study group consisted of 54 women in their third trimester of pregnancy with the diagnosis of PROM established by inspection of vaginal pooling while the control group consisted of 34 pregnant women with intact membranes. A cut-off value of 0.12 mg/dl was proposed for creatinine and its sensitivity, specificity, positive predictive value, negative predictive value, and accuracy in detecting PROM based on the aforementioned cut-off value were calculated to be 100%. They concluded that vaginal fluid creatinine measurement is cheaper and faster than other methods, and has higher sensitivity and specificity to establish an accurate diagnosis.[93] In a recent cross-sectional study by Kuruoğlu et al (2019), a statistically significant difference was found between the creatinine levels of vaginal lavage fluid of PPROM and non-PPROM patients. They found the mean creatinine level in vaginal flushing fluid was 0.39 (0.31) mg/dl in the PPROM group, and 0.04 (0.10) mg/dl in the non-PPROM group.

Veena Ramasamy et al in their study found that the optimal cut-off value of vaginal fluid creatinine to detect PPROM arrived based on ROC curve

analysis was ≥0.3 mg/dL. The mean vaginal fluid creatinine in group I was 1.097 mg/dL, in group II was 0.3 mg/dL, and in group III was 0.068 mg/dL. This study demonstrates that vaginal fluid creatinine could accurately diagnose a PPROM with a sensitivity, specificity, positive predictive value, and negative predictive value of 98.36, 100, 100, and 97.14%, respectively.[94]

MATERIALS AND METHODS

This was a prospective case-control study conducted on 150 pregnant women in the Department of Obstetrics and Gynaecology in collaboration with the Department of Biochemistry at Dayanand Medical College and Hospital, Ludhiana which is a tertiary care hospital. Informed consent in the patient's language was taken from all pregnant women who participated in the study. The sample size was calculated based on the accuracy level of diagnosis of PPROM by the measurement of vaginal fluid urea and creatinine.

SOURCE OF DATA

Pregnant women with singleton live fetuses (without any abnormality) coming to the labour room and willing to participate in the study were taken into our study. The gestational age of pregnancy of the women in our study was in between 28 weeks to 36 weeks 6 days period of gestation. A detailed history of the nature and type of discharge per vagina of the pregnant women participating in the study was taken. All the participants underwent general examination, abdominal examination, and sterile per speculum examination to look for any fluid coming out of the cervix or pooling of fluid in the posterior fornix. If the amniotic fluid was meconium stained or blood stained then these patients were excluded from this study. 150 pregnant women were taken in our study. These women were divided into three groups with 50 women in each group.

Group A-. Women with complaints of leaking per vagina, confirmed by visualization of clear liquid either in the posterior fornix or coming out from the cervix by per speculum examination.

Group B- Women with a history of leaking per vagina but no demonstrable active leaking on speculum examination, even after Valsalva maneuvers (women with suspected PPROM)

Group C- All the pregnant women in our study gave no history of leaking per vagina (women with no PPROM). This was taken as the Control group.

INCLUSION CRITERIA:

- Women with a singleton pregnancy.
- Gestation age between 28weeks-36weeks 6Days.
- Women with confirmed leaking /suspected leaking with no labour pains.

EXCLUSION CRITERIA:

- Multiple pregnancies
- Congenital malformation of the fetal urinary system
- Patients in labour
- Intrauterine fetal demise
- Meconium blood-stained liquor
- Women not willing to participate in the study
- Any amount of vaginal bleeding
- History of chronic hypertension or preeclampsia
- Renal insufficiency patients

METHOD:- While doing the speculum examination 5 ml of sterile saline was pushed into the vagina with a disposable 5 ml syringe and 3 ml of the same fluid was aspirated back in the same sitting and sent for biochemical study in a sterile container. In Group 1 where active leaking was present, the pooled amniotic fluid was first cleaned with sterile gauze before pushing the normal saline. The collected sample was sent to the biochemistry lab of Dayanand Medical Collage and Hospital for analysis. This sample was first centrifuged at 3000 rpm for 10 minutes and then processed.

Urea was analyzed by the Urease method and Creatinine by Jaffe's alkaline Picrate method. Tests were performed in the Auto-analyser Cobas 8000 and values were noted

Table 6:-NORMAL RANGE OF UREA AND CREATININE:-[80,81]

	CREATININE(mg/dl)	**UREA(mg/dl)**
SERUM /BLOOD	0.5-1.0	5 -20
URINE [80,81]	10	300
AMNIOTIC FLUID [80,81]	≤ 3.5	≤ 30

STUDY SAMPLE:

Primary objective: Evaluation urea in vaginal fluid in pprom

The formula used is as under:

$n = (\sigma 12 + \sigma 22) (Z\alpha + Z\beta)^2/(m1 – m2)^2$

Where,

Zα = Value of standard normal variate corresponding to α level of significance (1.96)

Zβ = The standard normal deviate for desired power (1.645)

m = Average

σ = Standard deviation

Assumptions:

From the study conducted by Yousry O.S EI Maraghy et al[95] With the above assumptions the sample size for 95% confidence level & 95% power works out to 36 in each group. This number has been increased to 50 each group to allow for a predicted dropout from treatment.

The study was conducted on 150 pregnant women in labour ward with PPROM. Group-A Group-B, and Group-C, were admitted for a period of amenorrhea.

THE NUMBER OF CASES:- 150 pregnant women with 50 in each group.

STATISTICAL ANALYSIS: Data was described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases), and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups was done using ANOVA. For comparing categorical data, the Chi-square ($\chi 2$) test was performed and the exact test was used when the expected frequency is less than 5.A probability value (p-value) less than 0.05 was considered statistically significant. All statistical calculations was done using (Statistical Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Window.

OBSERVATIONS & RESULTS

This was a prospective case control study conducted in the Department of OBSTETRICS AND GYNAECOLOGY in collaboration with the Department of Biochemistry at DAYANAND MEDICAL COLLEGE AND HOSPITAL, Ludhiana which is a tertiary care hospital. Informed consent in the patient's language was taken from all pregnant women who participated in the study. The sample size was calculated based on the accuracy level of diagnosis of PRETERM PRELABOUR RUPTURE OF MEMBRANES (PPROM) by the measurement of vaginal fluid urea and creatinine values. A total of 150 pregnant women who met the inclusion criteria were recruited into the study with 50 women in each group.

GROUP A- The Study **(Cases)** Group included women with complaints of leaking per vagina, confirmed by visualization of clear liquid either in the posterior fornix or coming out from the cervix by per speculum examination

GROUP B- (Suspected) Included women with a history of leaking per vagina but no demonstrable active leaking on speculum examination, even after Valsalva maneuver (women with suspected PPROM leaking when the clinician is not sure.

GROUP C- (The Control Group) This group consisted of pregnant women who did not either have a history of leaking per vagina or leak on speculum examination.

DEMOGRAPHIC PARAMETERS-:

1. AGE
2. EDUCATION
3. OCCUPATION
4. ANTENATAL CARE
5. SOCIOECNOMIC STATUS
6. GRAVIDITY

AGE (YEARS)

Table 7: Distribution of women under study according to age in Years:-

		Group A		Group B		Group C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
Age group	< 25	5	10.0%	5	10.0%	4	8.0%	14	0.562	0.967
	26-30	24	48.0%	27	54.0%	26	52.0%	77		
	> 30	21	42.0%	18	36.0%	20	40.0%	59		
Total		50	100.0%	50	100.0%	50	100.0%	150		

Most of the women in these groups were between the ages of 26 and 30. Groups A, B and C each included 48.0%, 54.0%, and 52.0% of the participants. Out of 50 women in group A, 5 (10%) belonged to the under-25 age group and 21 (42%) to the over-30 age group. Out of 50 women in group B, 5 (or 10.0%) were under the age of 25, and 18 (or 36.0%) were above the age of 30. Of the 50 women in group C, 4 (8.0%) were under the age of 25 and 20 (40.0%) were above the age of 30. Overall, there were no statistically significant differences between the three groups, and all three groups were comparable (p-value 0.967).

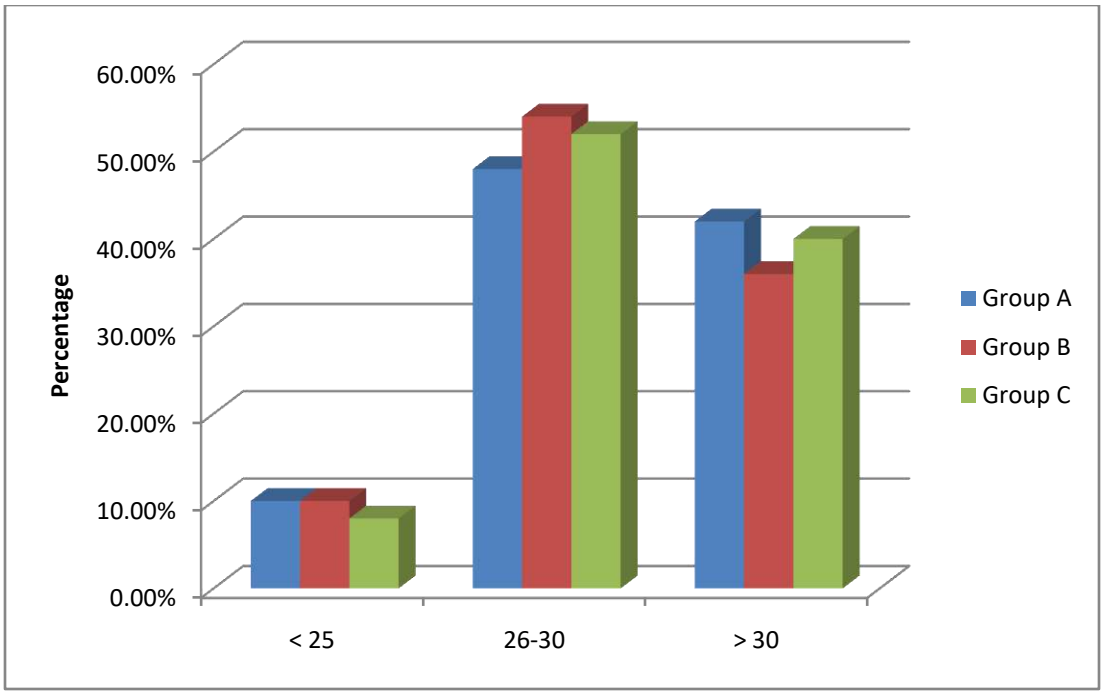


Figure1. Distribution of women under study according to age in years

Table 8: Distribution of women under study according to mean age in Years.

	Group A		Group B		Group C		F	p-value	A vs B	A vs C	B vs C
	Mean	SD	Mean	SD	Mean	SD			p-value	p-value	p-value
AGE(YR)	31.40	5.64	30.40	4.47	31.46	4.84	0.707	0.495	0.579	0.998	0.541

In our study, the mean age of group A was 31.40 +/-5.64 years compared to the mean age of 30.40+/-4.47 years in group B and 31.46 +/-4.84in group C. There was statistically no significant difference noted between the two groups. The age distribution in both groups was similar (p-value = 0.495)

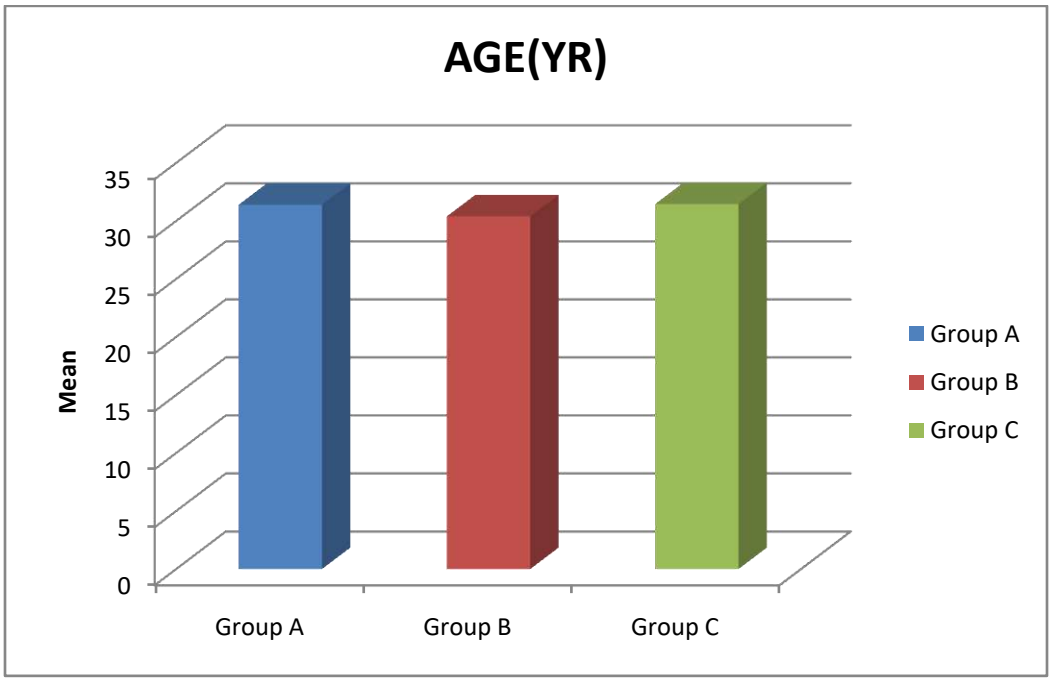


Figure2. Distribution of women according to mean Age

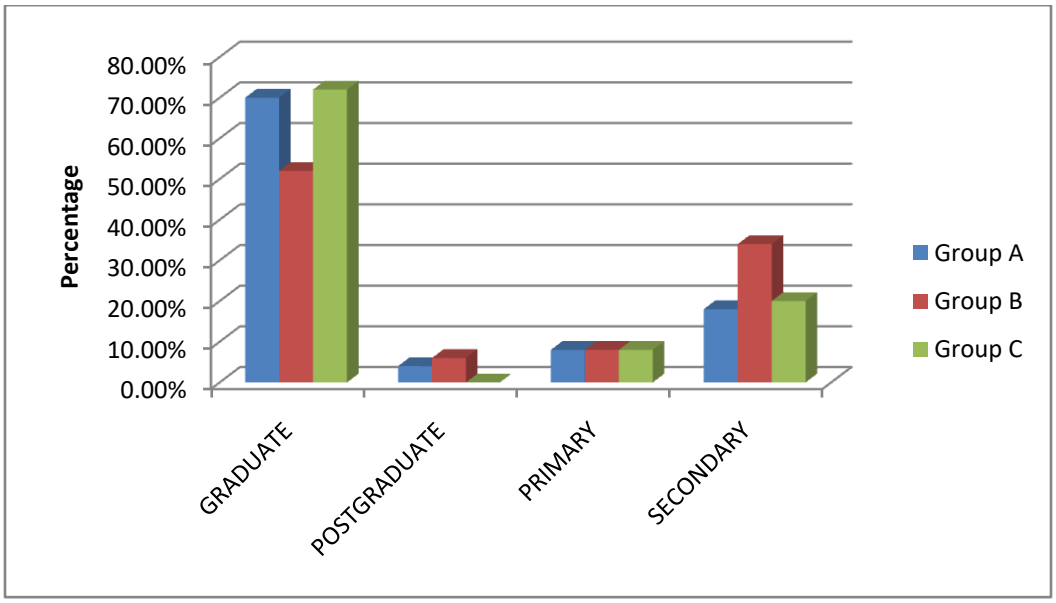
EDUCATION Table 9:- Distribution of women under study according to Education Status

		Group A		Group B		Group C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
EDUCATION	GRADUATE	35	70.0%	26	52.0%	36	72.0%	97	7.843	0.250
	POSTGRADUATE	2	4.0%	3	6.0%	0	0.0%	5		
	PRIMARY	4	8.0%	4	8.0%	4	8.0%	12		
	SECONDARY	9	18.0%	17	34.0%	10	20.0%	36		
Total		50	100.0%	50	100.0%	50	100.0%	150		

Among these groups; the majority of women were graduates 70.0% in group A, 52.0% in group B and 72.0% in group c. Out of 50 women in group A, 2(4.0%), 3(6.0%) group B and 0(00.0%) Group C were postgraduate. Out of 50 women in group A 4(8.0%), 4(8.0%) group B and 4(8.0%) group C had primary level education. Out of 50 women in group A 9(18.0%), 17(34.0%) group B and 10(20.0%) group C had secondary level education. For all Group a Group B and Group C.

Overall all three groups were comparable and there was statistically no significant difference between the two groups (p-value =0.250

Figure3. Distribution of women under study according to education status



OCCUPATION:-Table 10: Distribution of women under study according to occupation

		Group A		Group B		Group C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
OCCUPATION	GOVT JOB	11	22.0%	7	14.0%	10	20.0%	28	4.932	0.294
	HOUSEWIFE	19	38.0%	30	60.0%	24	48.0%	73		
	PVT JOB	20	40.0%	13	26.0%	16	32.0%	49		
Total		50	100.0%	50	100.0%	50	100.0%	150		

Among these groups; a majority of women were housewives 38.0% in group A, 60.0% in group B and 48.0% in group c. Out of 50 women in group A, 11(22.0%), 7(14.0%) in group B and 10(20.0%) Group C were a government employee. Out of 50 women in group A 20(40.0%), 13(26.0%) group B and 16(32.0%) group C were under private sector.

Overall all three groups were comparable and there was statistically no significant difference between the two groups (p-value =0.294

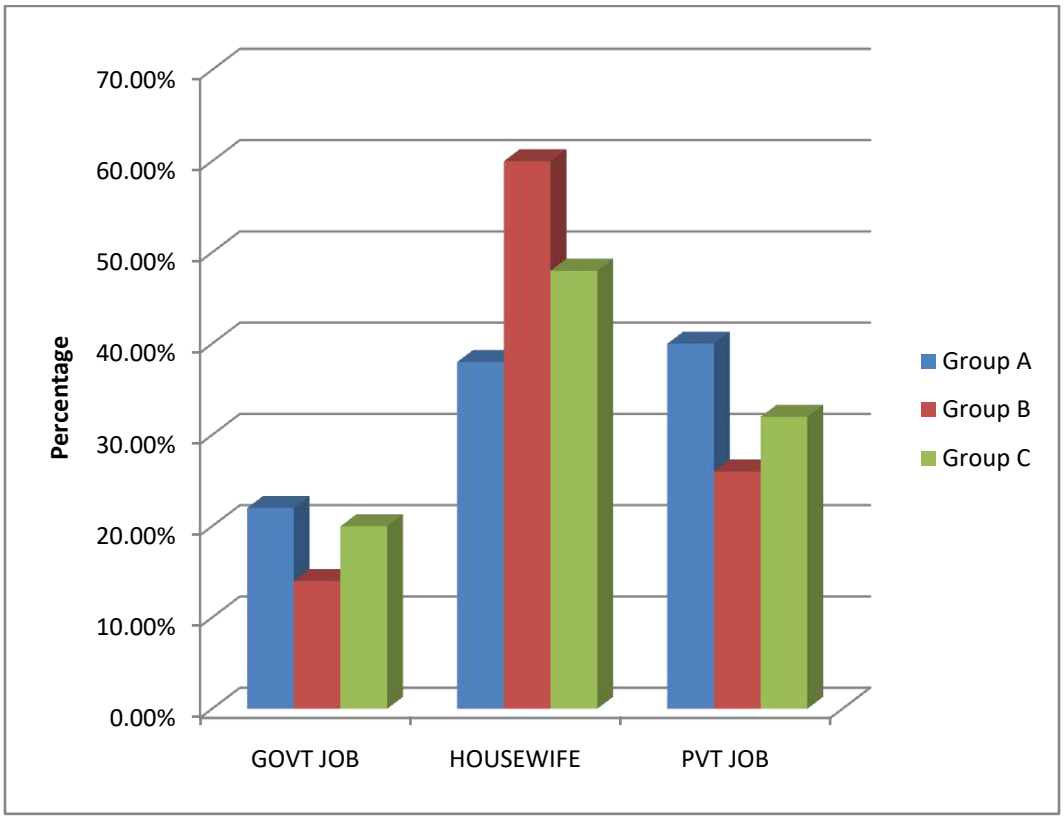


Figure4:Distribution of women under study according to occupation-

ANTENATAL CARE-:

Table 11: Distribution of women under study according to antenatal care

		Group A		Group B		Group C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
	BOOKED	45	90.0%	47	94.0%	43	86.0%	135	1.778	0.411
BOOKED /UNBOOKED	UNBOOKED	5	10.0%	3	6.0%	7	14.0%	15		
Total		50	100.0%	50	100.0%	50	100.0%	150		

In our study, 90.0% (n=45) of pregnancies in group A and 94.0% (n=47) in group B and 86% (43) of pregnancies in group C were booked cases. Group A 10.0% (n=5) pregnancies and 6.0% (n=3) pregnancies from group B and 14.0% (n=7) in group C were unbooked cases.There was statistically no significant difference in all groups (p-value=0.411)

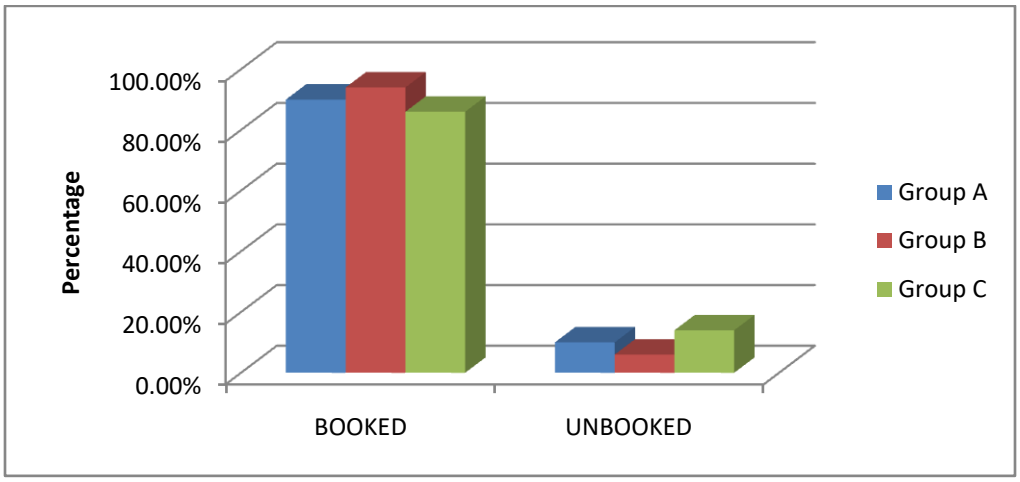


Figure5: Distribution of women under study according to antenatal care

SOCIOECONOMIC STATUS:- Distribution of women under study according to socioeconomic status-:

150 women of all groups were classified into the following 5 groups according to the Modified Kuppuswamy Scale

- Lower class(score: below 5)
- Upper lower class (score: 5-10)
- Lower middle class (score: 11-15)
- Upper middle class (score: 16-25)
- Upper class (score: 26-29)

SOCIOECONOMIC STATUS:- Table 12:- Distribution of women under study according to socio-economic.

		Group A		Group B		Group C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
SOCIOECONOMIC STATUS	LOWER CLASS	0	0.0%	3	6.0%	1	2.0%	4	12.044	0.149
	LOWER MIDDLE CLASS	19	38.0%	21	42.0%	19	38.0%	59		
	UPPER CLASS	9	18.0%	6	12.0%	14	28.0%	29		
	UPPER LOWER CLASS	6	12.0%	1	2.0%	4	8.0%	11		
	UPPER MIDDLE CLASS	16	32.0%	19	38.0%	12	24.0%	47		
Total		50	100.0 %	50	100.0%	50	100.0 %	150		

Among these groups; a majority of women belonged to the lower middle class 38.0% (n=19) in group A, 42.0% (n=21) in group B and 38.0% (n=19) in group C. Out of 50 women in group A, 0.0%(n=0), 6.0%(n=3) group B and 2.0% (n=1) group C were belonged to lower class. Out of 50 women in group A 32.0% (n=16), 38.0%(n=19) in group B and 24% (n=12) in group C belonged to the upper middle class. Out of 50 women in group A 18.0% (9), 12.0%(n=6) in group B and 28.0%(n=14) in group C belonged to the upper class. Out of 50 women in group A 12.0%(n=6), 2.0%(n=1) group B, and 8.0%(n=4) in group C belonged to the upper lower class.

Overall all three groups were comparable and there was statistically no significant difference between the two groups (p-value =0.149)

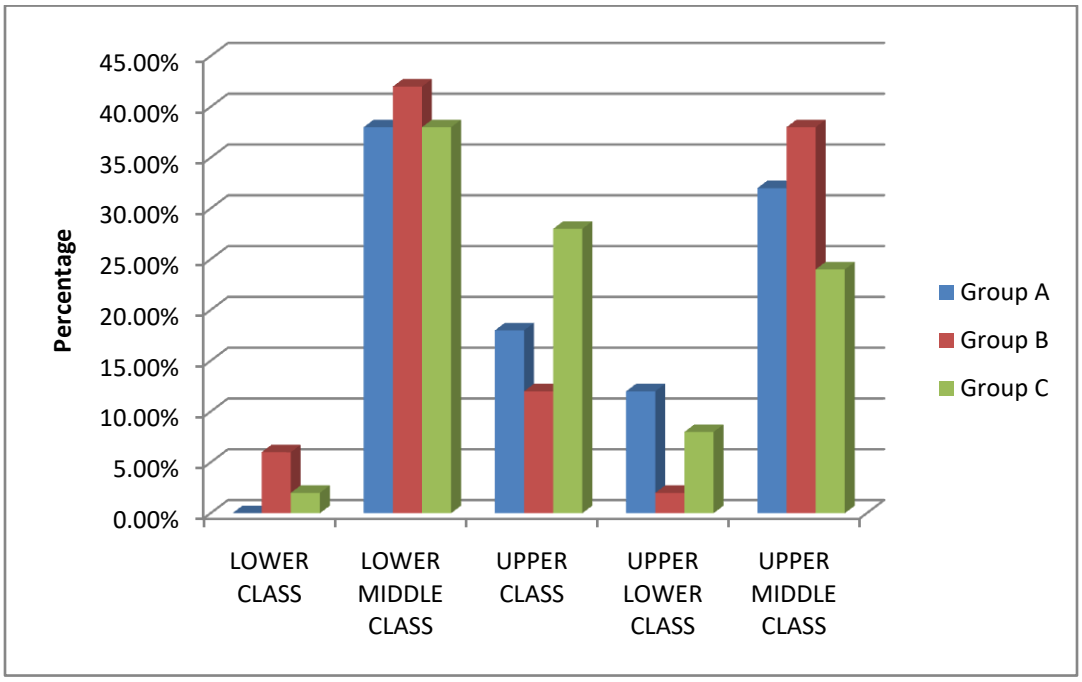


Figure 6:- Distribution of women under study according to socio-economic status

GRAVIDITY:- TABLE 13:-Distribution of women under study according to gravidity

		Group A		Group B		Group A		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
OBSTETRICS HISTORY (PRIMIGRAVIDA/ MULTIGRAVIDA)	MULTI	24	48.0%	30	60.0%	24	48.0%	78	1.923	0.382
	PRIMI	26	52.0%	20	40.0%	26	52.0%	72		
Total		50	100.0%	50	100.0%	50	100.0%	150		

In group A, 52% (n=26) women were Primigravida and 48. 0% (n=24) women were Multigravida while in group B, 40.0% (n=20) women were Primigravida and 60.0% (n=30) women were Multigravida. In group C, 48% (n=24) women were Primigravida and 52.0% (n=26) women were Multigravida hence the distribution in both groups was similar.

There was statistically no significant difference in gravidity between the two groups (p value=0.382)

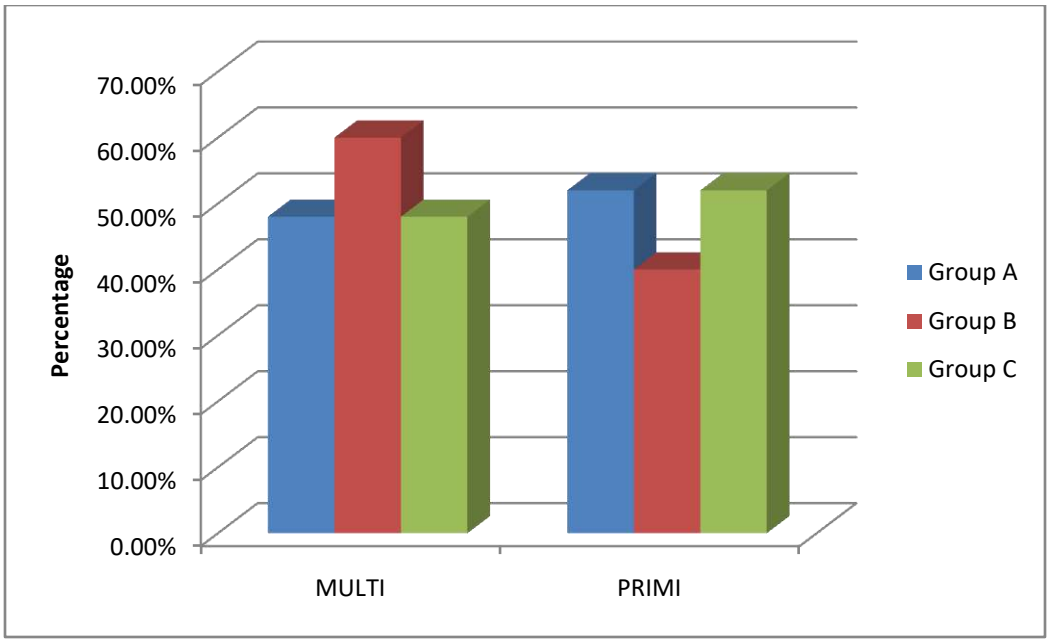


Figure 7.Distribution of women under study according to gravidity

MATERNAL FACTORS:-

The following maternal parameters were studied for all groups:

- Gestational age
- Duration of leaking
- Colour of liquor
- labor pains
- Amniotic Fluid Index (AFI)
- vaginal fluid urea values
- vaginal fluid creatinine values
- Association of UTI
- Association of genital infection

GESTATION AGE-: TABLE 14:-Distribution of groups under study according to gestation age

gestation			Group A		Group B		Group C		Total	Chi-square value	p-value
			No. of cases	%age	No. of cases	%age	No. of cases	%age			
28-30	LEAKING	A	0	0.0%	0	0.0%	1	100.0%	1	22.000	0.001
		P	6	100.0%	0	0.0%	0	0.0%	6		
		S	0	0.0%	4	100.0%	0	0.0%	4		
	Total		6	100.0%	4	100.0%	1	100.0%	11		
30-32	LEAKING	A	0	0.0%	0	0.0%	1	100.0%	1	24.000	0.001
		P	8	100.0%	0	0.0%	0	0.0%	8		
		S	0	0.0%	3	100.0%	0	0.0%	3		
	Total		8	100.0%	3	100.0%	1	100.0%	12		

32-34	LEAKING	A	0	0.0%	0	0.0%	11	100.0%	11	52.000	0.001
		P	6	100.0%	0	0.0%	0	0.0%	6		
		S	0	0.0%	9	100.0%	0	0.0%	9		
	Total		6	100.0%	9	100.0%	11	100.0%	26		
> 34	LEAKING	A	0	0.0%	0	0.0%	37	100.0%	37	202.000	0.001
		P	30	100.0%	0	0.0%	0	0.0%	30		
		S	0	0.0%	34	100.0%	0	0.0%	34		
	Total		30	100.0%	34	100.0%	37	100.0%	101		

[A- ABSENT , P - PRESENT , S- SUSPECT]

Among the three groups the majority of patients with leaking belong to a gestation age of more than 34 weeks 30(100.0%) patients in Group A and 34 (100.0%) in Group B suspected, at 32 -34 weeks 6 (100.0%) in Group A and 9 (100.0%) in Group B, at 30-32weeks 8(100.0%) Group A and 3(100.0%) in Group B, at 28-30 weeks 6(100.0%) Group A and 4(100.0%) in Group B. There was a statistically significant difference between the three groups with p-value =0.001

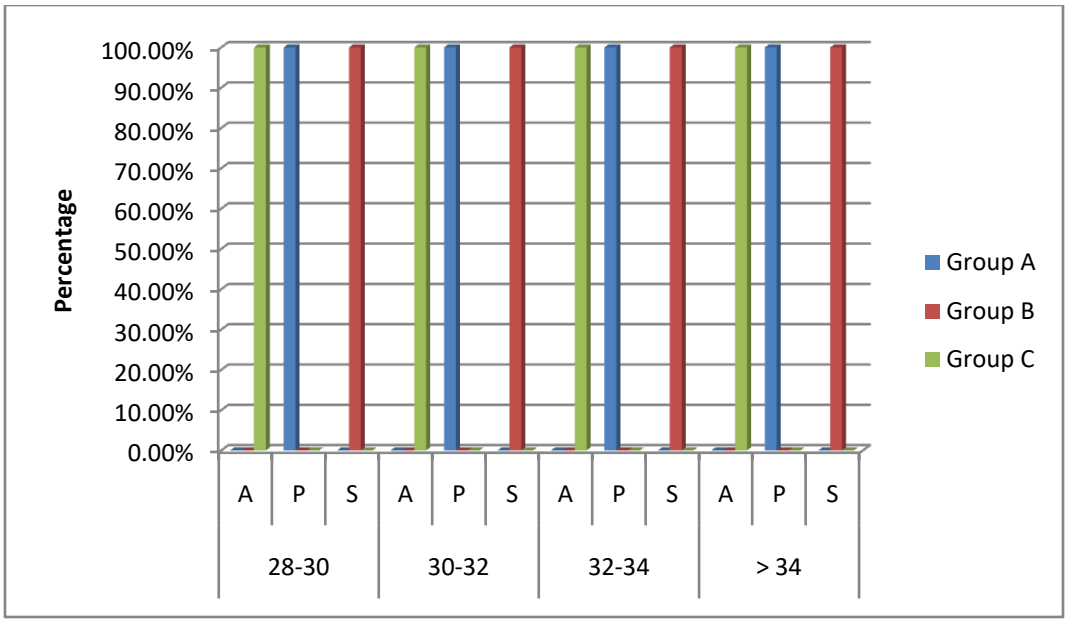


FIGURE 8:- Distribution of groups under study according to gestation age

DURATION OF LEAKING:-Table 15 Distribution of 3 groups under study is according to duration of leaking.

	Group A		Group B		Group C		F	p-value	A vs B	A vs C	B vs C
	Mean	SD	Mean	SD	Mean	SD			p-value	p-value	p-value
LEAKING Duration(HOURS)	13.28	20.06	16.83	23.93	.	.	0.584	0.447			

Majority of patients with confirmed leaking presented after mean Duration of 13.26 hours and with suspected leaking presented after a mean duration of 16.83 hours.

There was statistically no significant difference in gravidity between the two groups (p-value=0.447)

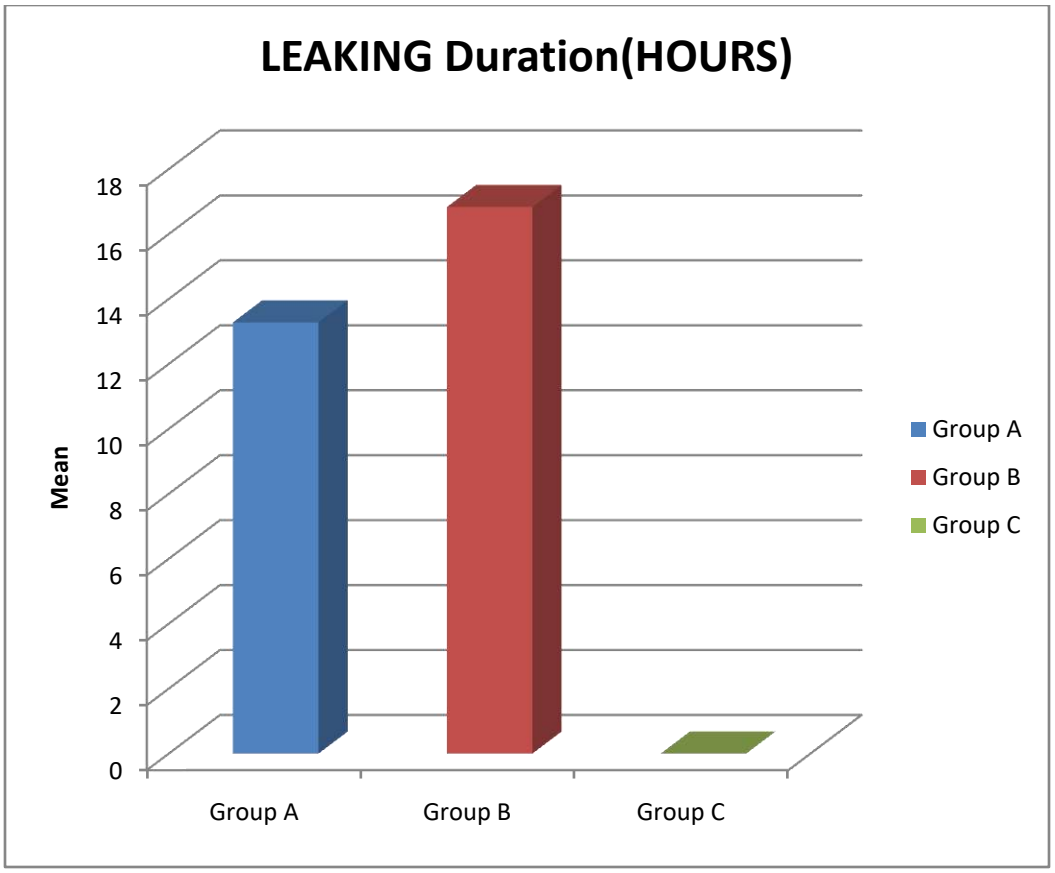


FIGURE 9:-Distribution of 3 groups under study according to duration of leaking

ULTRASOUND:- Table 16 Difference in amniotic fluid index among three groups

		Group A		Group B		Group c		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
Amniotic fluid(NORMAL/DECREASED)	DECREASED	49	98.0%	2	4.0%	0	0.0%	51	137.077	0.001
	NORMAL	1	2.0%	48	96.0%	50	100.0%	99		
Total		50	100.0%	50	100.0%	50	100.0%	150		

Among these groups; 98.0% in group A, 4.0% in group B and 0.0% in group c had decreased amniotic fluid index on ultrasound. Out of 50 women in group A 1(2.0%), 48(96.0%) in group B and 50(100.0%) in group C had a normal amniotic fluid index on ultrasound. Overall in all 3 groups, there was a statistically significant difference in Amniotic fluid index (p-value =0.001)

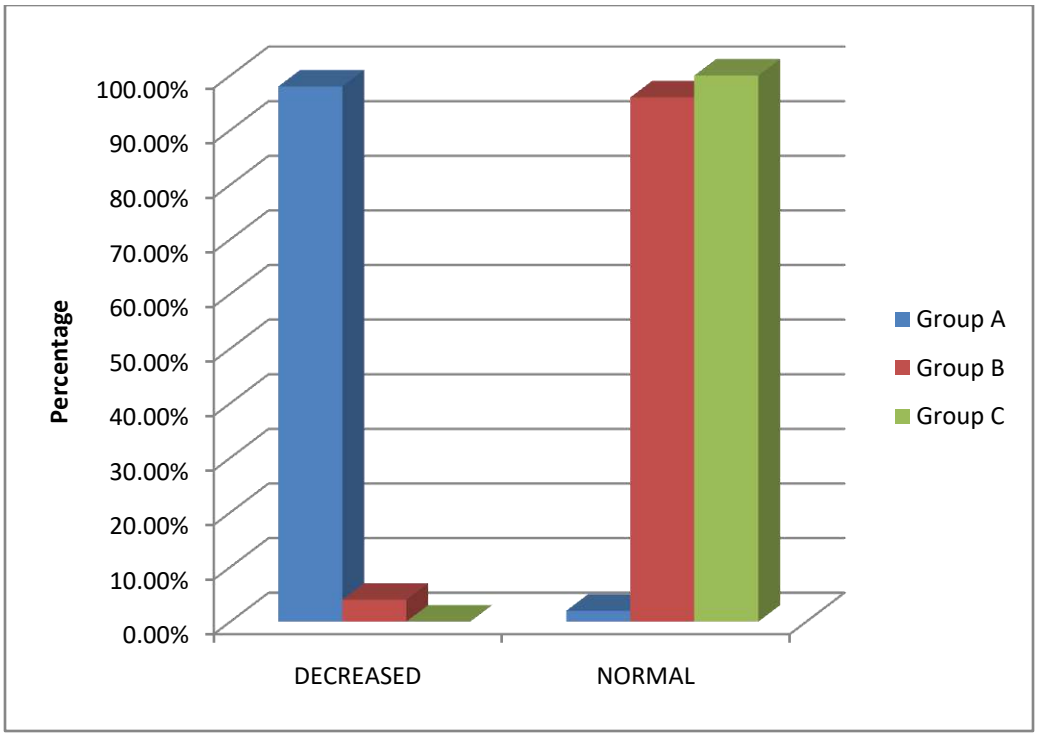


Figure 10:- Difference in amniotic fluid index among three groups

Table 17 Difference in mean AFI among three groups

	Group A		Group B		Group C		F	p-value	A vs B	A vs C	B vs C
	Mean	SD	Mean	SD	Mean	SD			p-value	p-value	p-value
USG FWB (AMNIOTIC FLUID INDEX)	5.16	1.79	12.88	3.56	13.54	3.01	130.533	0.001	0.001	0.001	0.488

Among these groups; the mean amniotic fluid index was 5.16+/-1.79 in group A, 12.88+/-3.56 in group B and 13.55+/-3.01 in Group C Overall in all 3 groups, there was a statistically significant difference in the mean amniotic fluid index (p-value =0.001) If compare GROUP A & B (P -value -0.001) that is a statistically significant difference. If compare GROUP A & C (P -value -0.001) that is a statistically significant difference. If compare GROUP B &C (p -value -0.488) that is statistically insignificant.

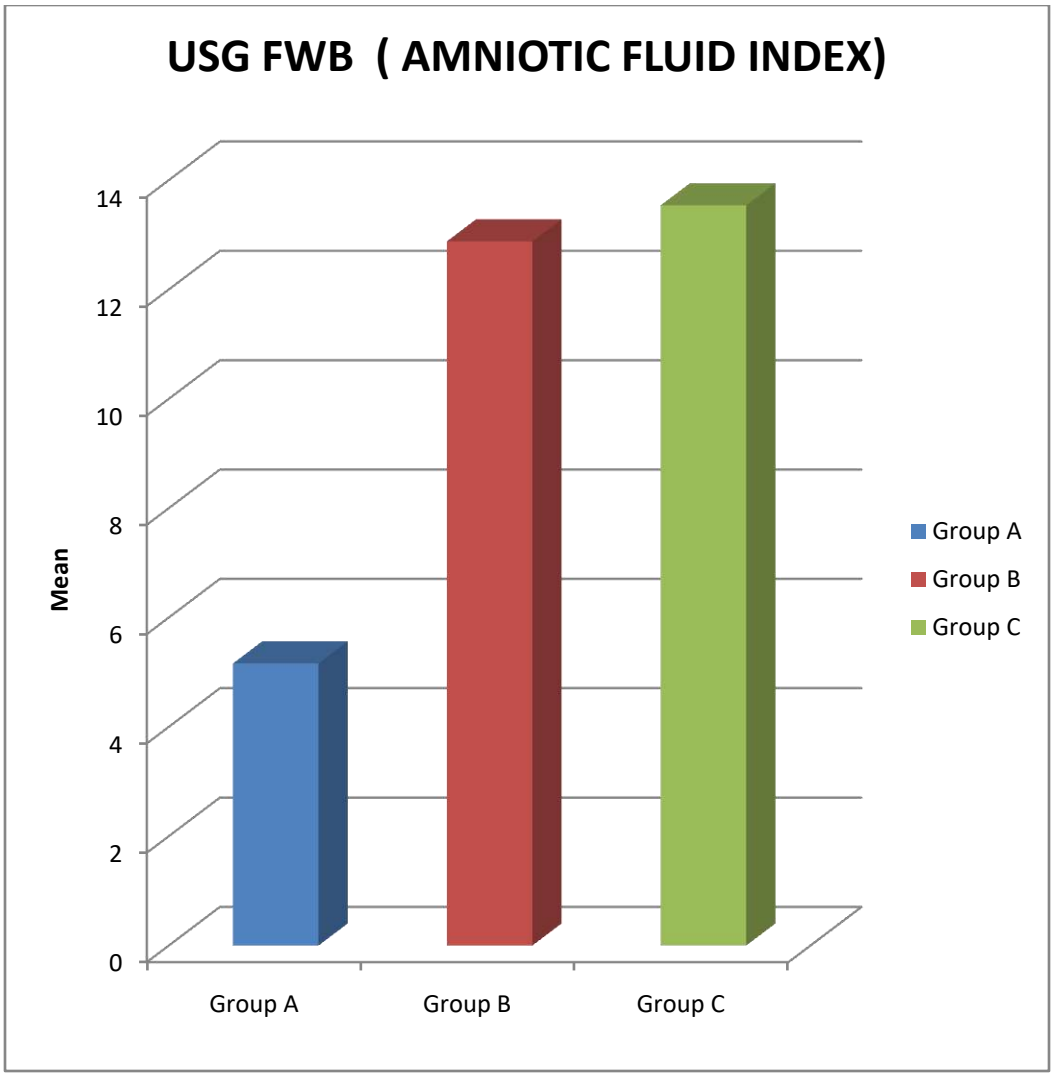


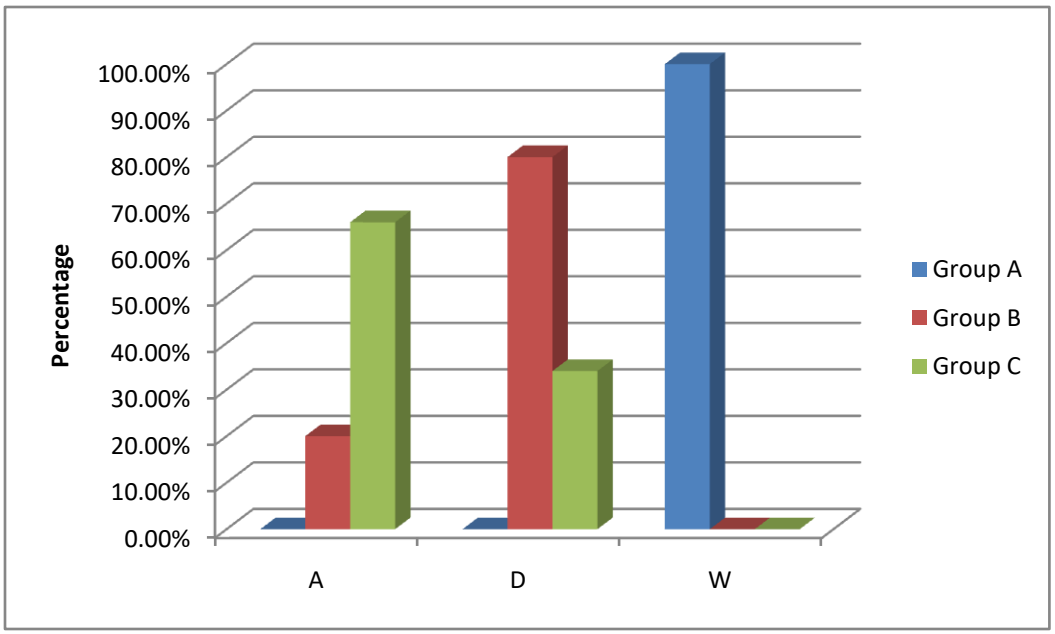
Figure 11:-Difference in mean AFI among three groups

LOCAL EXAMINATION (VULVAL PAD):- TABLE 18 Difference in local examination among three groups:-

		Group A		Group B		Group C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
VULVAL PAD ABSENT(A)/DRY(D)/WET(W)	A	0	0.0%	10	20.0%	33	66.0%	43	182.375	0.001
	D	0	0.0%	40	80.0%	17	34.0%	57		
	W	50	100.0%	0	0.0%	0	0.0%	50		
Total		50	100.0%	50	100.0%	50	100.0%	150		

[A = absent , D = dry , W = wet]

Among these groups; 100.0% in group A, 0.0% in group B and 0.0% in group C had a wet vulval pad on local examination. Out of 50 women in group A 0(0.0%), 40(80.0%) in group B and 17(34.0%) in group C had a dry vulval pad on local examination. Out of 50 women in group A 0(0.0%), 10(20.0%) in group B and 33(66.0%) in group C had an absent vulval pad on local examination. There was a statistically significant difference among three groups (p-value =0.001).



[A = ABSENT, D =DRY, W =WET]

Figure 12:- Difference in local examination among three groups

PER- SPECULUM EXAMINATION:- Table19:- Difference in Per-speculum examination among three groups

		Group A		Group B		Group C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
PER SPECULUM POOLING (+/-)	-	1	2.0%	50	100.0%	50	100.0%	101	145.545	0.001
	+	49	98.0%	0	0.0%	0	0.0%	49		
Total		50	100.0%	50	100.0%	50	100.0%	150		

Among these groups; 98.0% in group A, 0.0% in group B and 0.0% in group c had pooled per speculum examination. Out of 50 women in group A 1(2.0%), 50(100.0%) group B and 50(100.0%) Group C had no pooling per speculum examination. Overall in all 3 groups, there was a statistically significant difference between three groups (p-value =0.001)

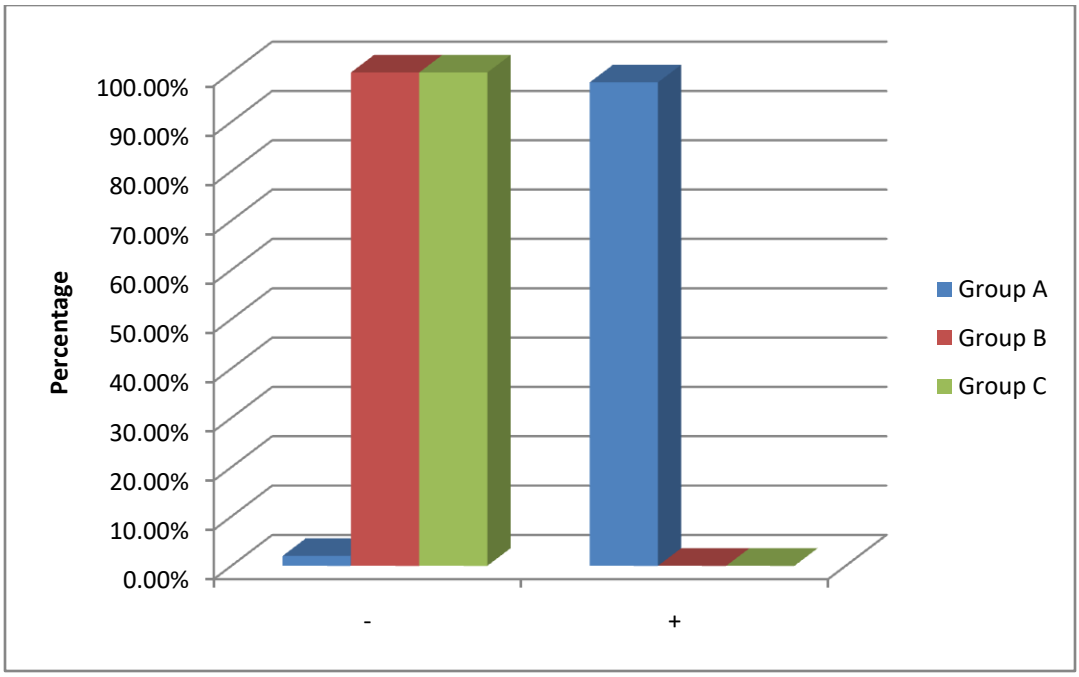


Figure 13:- Difference in Per-speculum examination among three groups

Table 20:-Difference between mean vaginal fluid urea and creatinine among three groups

	Group A		Group B		Group c		F	p-value	A vs B	A vs C	B vs C
	Mean	SD	Mean	SD	Mean	SD			p-value	p-value	p-value
UREA	9.16	6.01	2.06	0.82	0.75	0.48	82.875	0.001	0.001	0.001	0.152
CREATININE	0.52	0.47	0.13	0.08	0.18	0.27	22.270	0.001	0.001	0.001	0.698

Among these groups; the mean urea in the vaginal fluid was 9.16+/-6.01 in group A, 2.06+/-0.82 in group B and 0.75+/-0.48 in group C. Among these groups; mean creatinine in the vaginal fluid was 0.52+/-0.47 in group A, 0.13+/-0.08 in group B and 0.18+/-0.27 in Group C Overall in all 3 groups, there was a statistically significant difference in mean vaginal fluid urea and creatinine levels (p-value =0.001) If comparing GROUP A & B vaginal fluid urea and creatinine (p -value -0.001) that is a statistically significant difference. If comparing GROUP A & C vaginal fluid urea and creatinine (p -value -0.001) that is a statistically significant difference. If comparing GROUP B & C vaginal fluid urea (p -value -0.152) for urea and (0.698) for creatinine that is statistically insignificant.

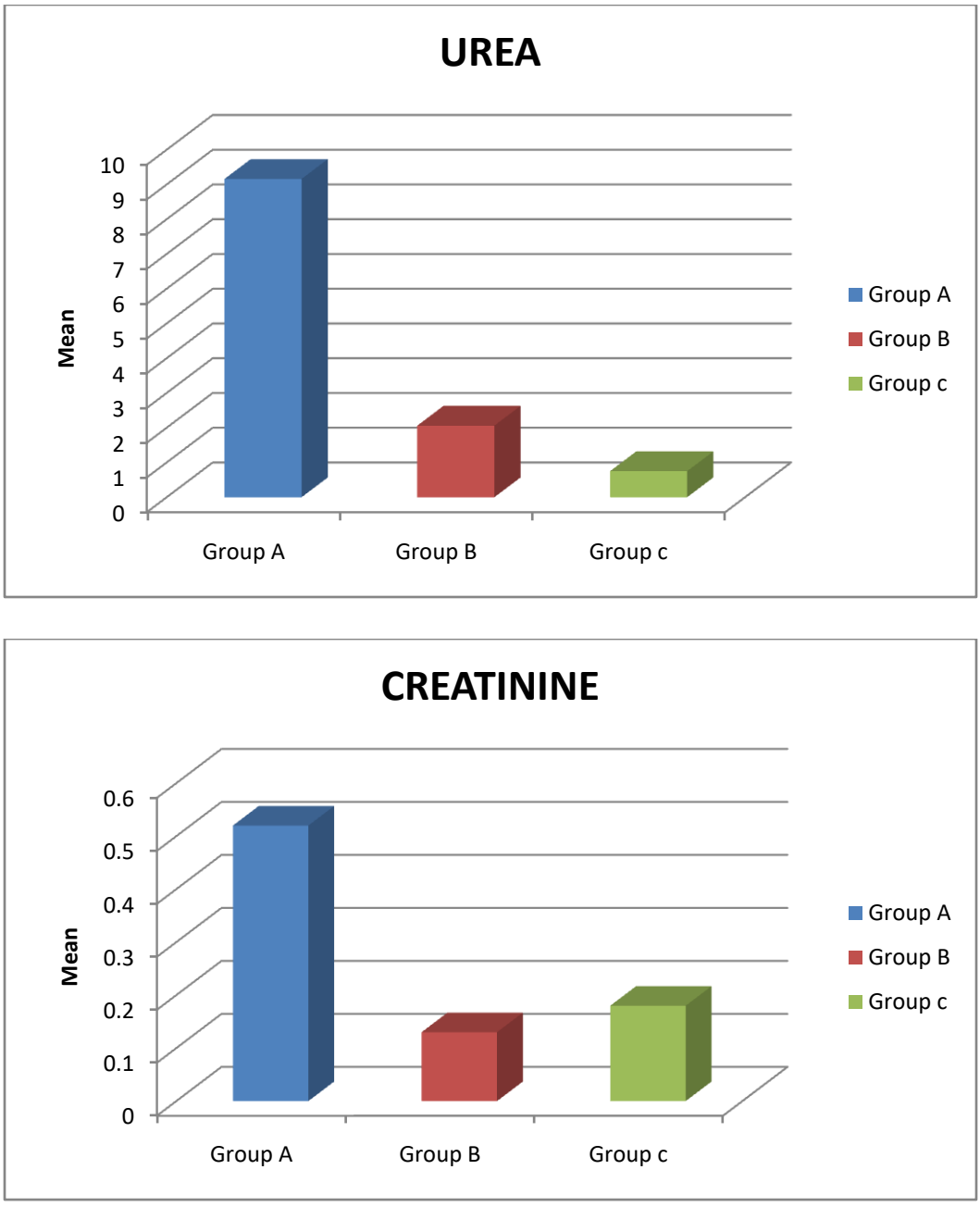


Figure 14:-Difference between mean vaginal fluid urea and creatinine among three groups

Table 21:- Different urea levels among 3 groups

		Group A		Group B		Group C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
Urea	**< 5**	19	38.0%	50	100.0%	50	100.0%	119	78.151	0.001
	5.1-10	15	30.0%	0	0.0%	0	0.0%	15		
	10.1-15	12	24.0%	0	0.0%	0	0.0%	12		
	15.1-20	2	4.0%	0	0.0%	0	0.0%	2		
	20.1-25	2	4.0%	0	0.0%	0	0.0%	2		
Total		50	100.0%	50	100.0%	50	100.0%	150		

The majority of patients in group A have urea values between 5 to 25.IN Group B and C all patients have urea values less than 5 In all the 3 groups there was a statistically significant difference in vaginal fluid Urea values (p-value =0.001).

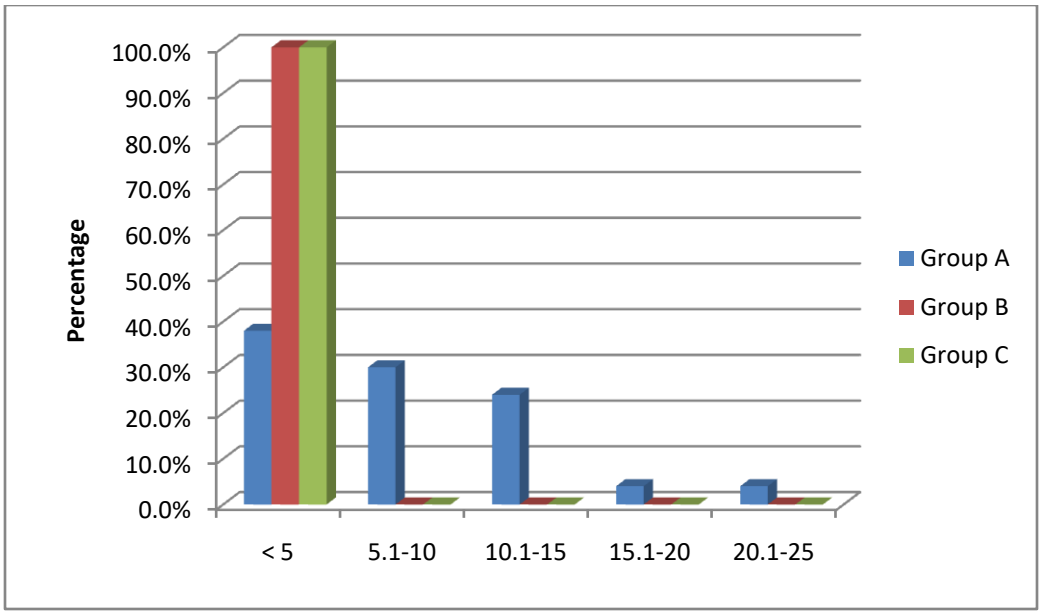


FIGURE 15:- Different urea levels among 3 groups

Table 22:- Different Creatinine levels among three groups

		Group A		Group B		Group C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
Creatinine	< 0.1	3	6.0%	27	54.0%	30	60.0%	60	81.655	0.001
	0.1-0.2	12	24.0%	19	38.0%	18	36.0%	49		
	0.2-0.3	8	16.0%	4	8.0%	0	0.0%	12		
	0.31-0.50	7	14.0%	0	0.0%	0	0.0%	7		
	0.51-0.70	8	16.0%	0	0.0%	0	0.0%	8		
	0.71-0.90	8	16.0%	0	0.0%	0	0.0%	8		
	0.91	4	8.0%	0	0.0%	2	4.0%	6		
Total		50	100.0%	50	100.0%	50	100.0%	150		

The majority of patients in group A had creatinine values between 0.21 to 0.91IN Group B and C all patients had creatinine values between < 0.10 Overall in all 3 groups, there was a statistically significant difference in mean vaginal fluid creatinine values (p-value =0.001).

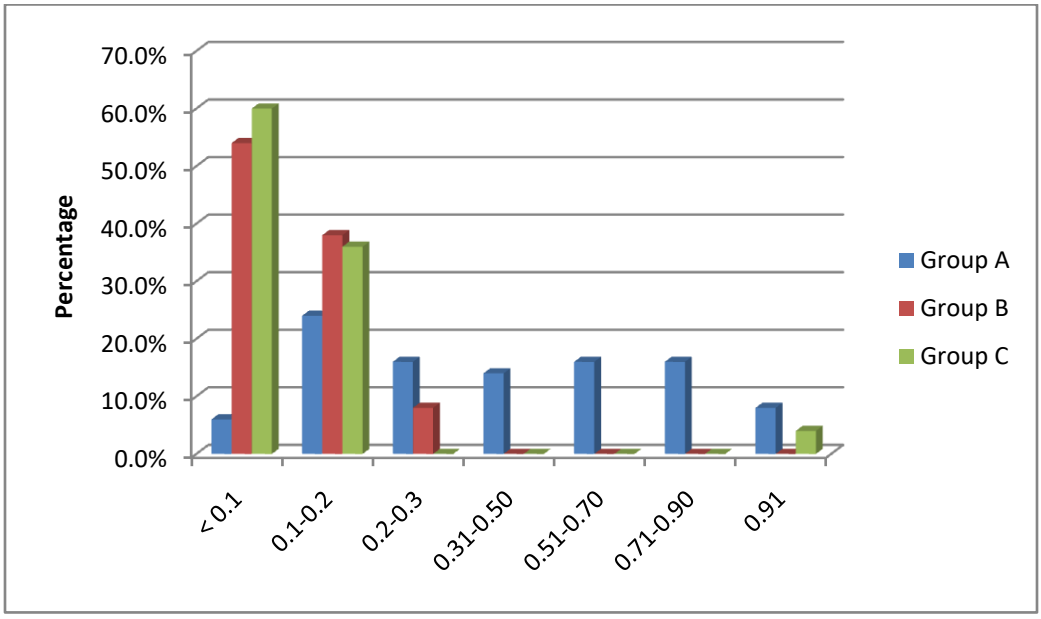


Figure 16:- Different Creatinine levels among three groups

URINE CULTURE:- Table 23:- Distribution of women under study according to Urine Culture.

		Group A		Group B		Group C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
URINE CULTURE	GROWTH -	28	56.0%	47	94.0%	45	90.0%	120	27.25	0.001
	GROWTH +	22	44.0%	3	6.0%	5	10.0%	30		
Total		50	100.0%	50	100.0%	50	100.0%	150		

Among three groups 22(44.0%) women in group A, 3(6.0%) in group B, 5(10.0%) had positive urine culture report. In 50 women 28 (56.0%) women in group A, 47(94.0%) in group B, 45(90.0%) had negative urine culture report. Overall all three groups there was a statistically significant difference between the three groups (p-value =0.001)

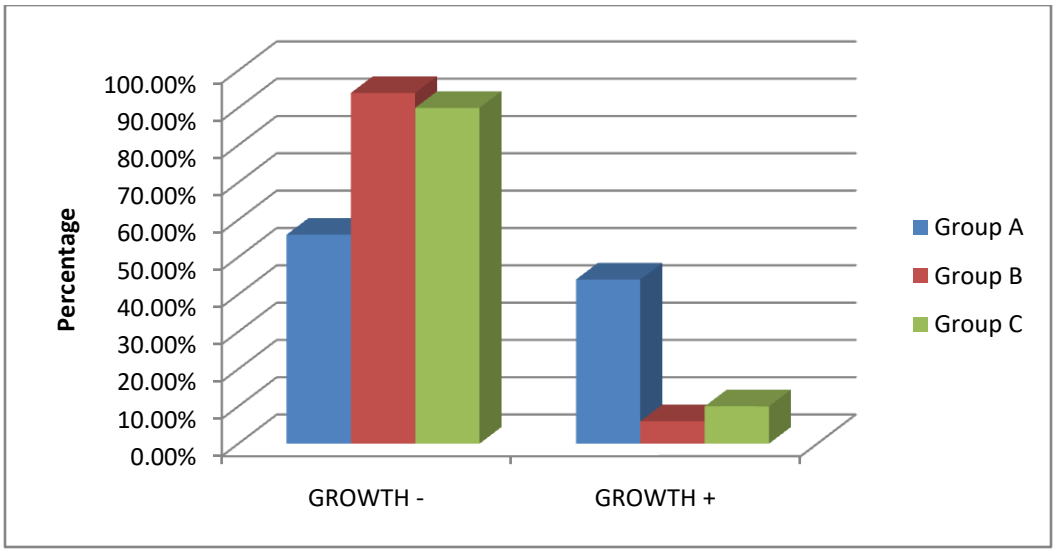


FIGURE 17:- Distribution of women under study is according to Urine Culture.

HIGH VAGINAL SWAB:- Table 24:- Distribution of women under study accoding to HIGH VAGINAL SWAB

		Group A		Group B		Group C		Total	Chi-square value	p-value
		No. of cases	%age	No. of cases	%age	No. of cases	%age			
HIGH VAGINAL SWAB	-	27	54.0%	49	98.0%	50	100.0%	126	53.098	0.001
	+	23	46.0%	1	2.0%	0	0.0%	24		
Total		50	100.0%	50	100.0%	50	100.0%	150		

Among three groups 23(46.0%) women in group A, 1(2.0%) in group B, 50(100.0%) had positive urine culture report. In 50 women 27(54.0%) women in group A, 49(98.0%) in group B, 50(100.0%) had negative urine culture report. Overall all three groups there was a statistically significant difference between the three groups (p-value =0.001)

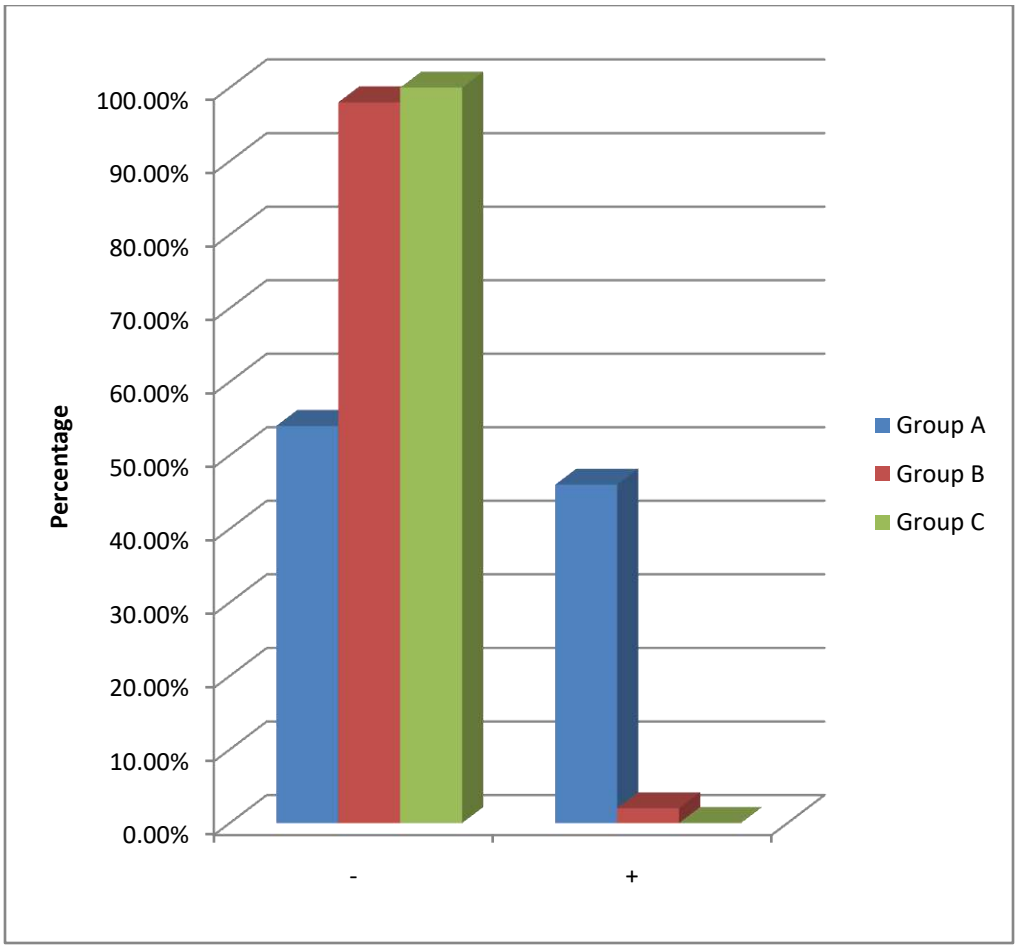


Figure 18:- Distribution of women under study according to HIGH VAGINAL SWAB

Table:- 25 ROC and AREA UNDER CURVE FOR GROUP –A [CASES]

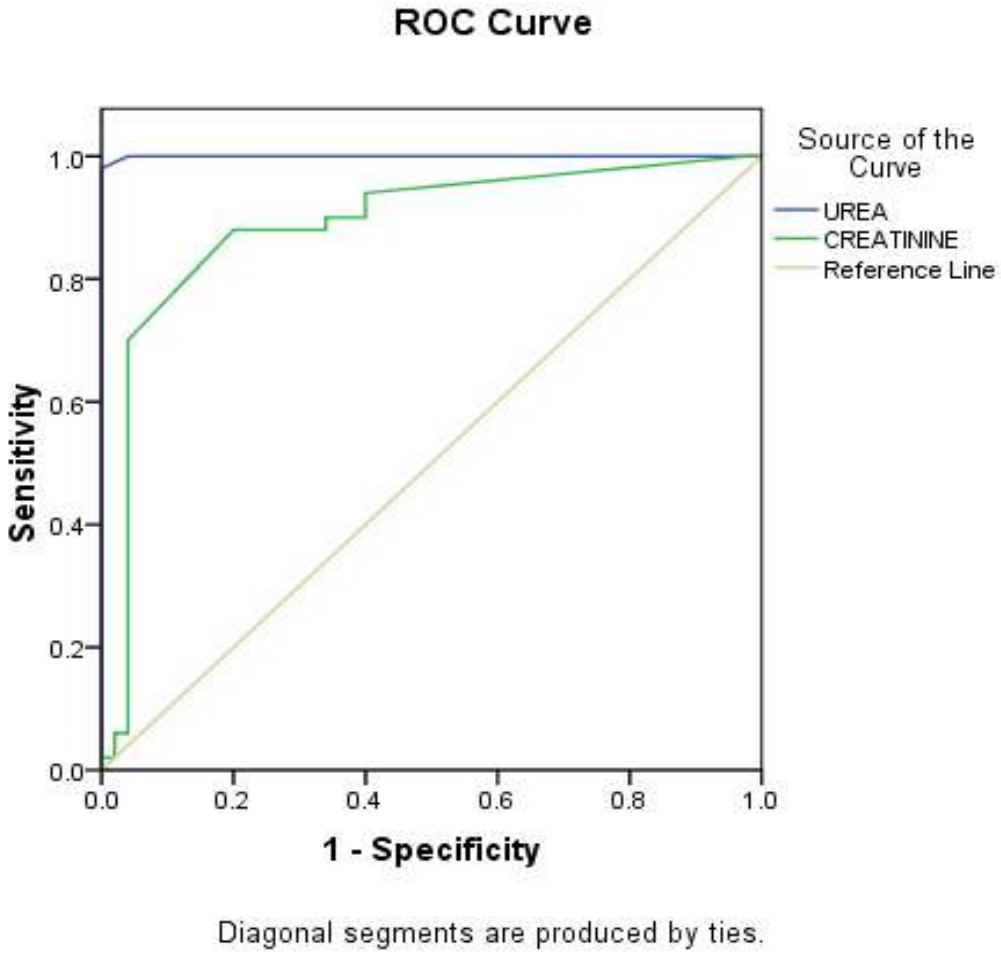
Test Result Variable(s)	Area	Std. Error	p-value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
UREA	1.000	.001	.000	.000	1.000
CREATININE	.888	.036	.000	.817	.959

A ROC curve showing urea is the best predictor of cases with an area under the curve of 1.0 with a confidence interval of 0.00 to 1.00 with a significant p-value < 0.001.

Creatinine is also a good predictor of cases with an area under the curve of 0.88 with a confidence interval of 0.81 to 0.959 with a significant p-value> 0.001.

In our study, the cutoff value for urea in patients in the group with the confirmed leak is ≥ 2.50 mg/dl with a sensitivity of 98% and a specificity of 100%. The cutoff value for creatinine in the group with confirmed leakage is ≥0.2 mg/dl with a sensitivity of 88% and a specificity of 80%.

Figure:- 19 RECEIVER OPERATOR CURVE GROUP-A[CASES]



AREA UNDER CURVE GROUP –B [SUSPECT]

Table 26:-Area Under the Curve

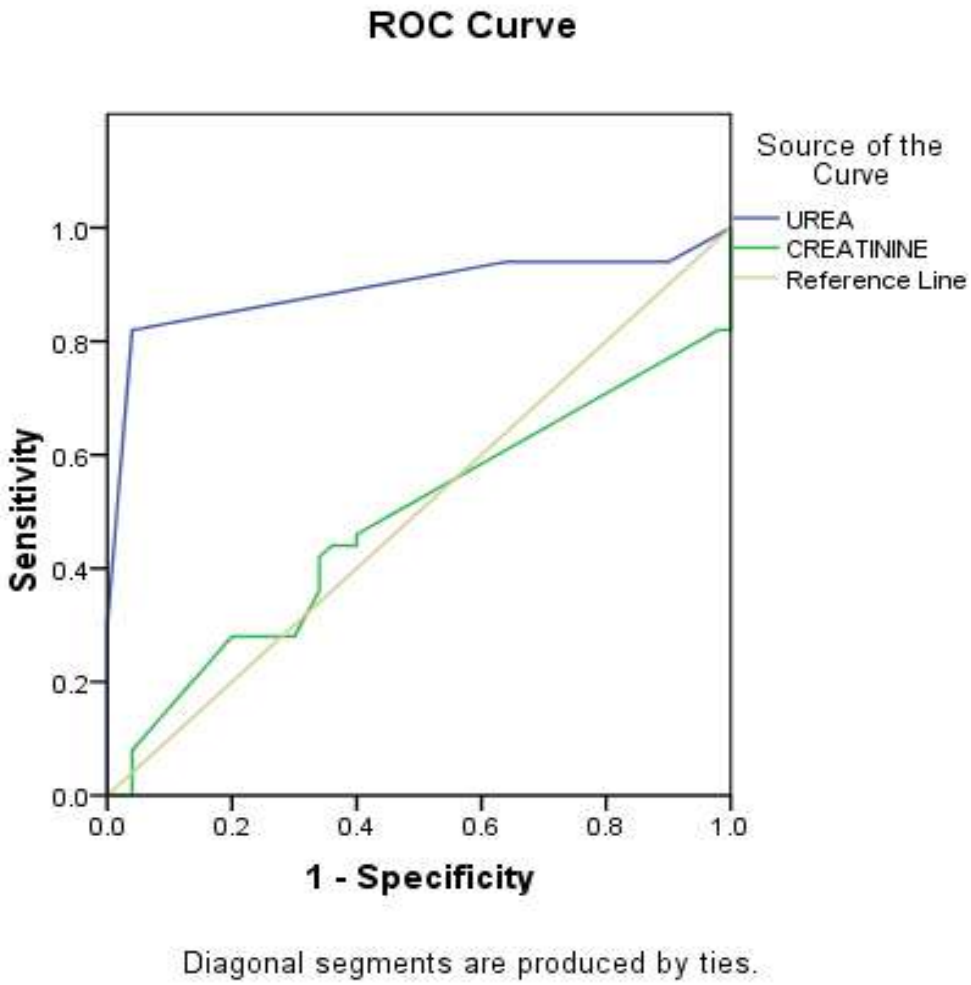
Test Result Variable(s)	Area	Std. Error	P value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
UREA	.892	.037	.000	.819	.964
CREATININE	.483	.059	.775	.368	.599

A ROC curve showing urea is the best predictor to predict suspects with the area under curve 0.89 with a confidence interval of 0.819 to 0.964 with a significant p-value <0.001

A ROC curve showing creatinine can also be the predictor for suspects with the area under curve 0.4 with a confidence interval of 0.36 to 0.59 with a significant p-value< 0.001 in our study, the cutoff value of urea in suspected leaking group patients is ≥1.5 mg/dl with a sensitivity of 82% and specificity of 96%.

The cutoff value for creatinine in the suspected leaking group is ≥ 0.1 mg/dl with a sensitivity of 46% and specificity of 60%.

Figure 20:- RECEIVER OPERATER CURVE GROUP –B [SUSPECT]



DISCUSSION

Preterm pre-labour rupture of the membranes is one of the most common complication that significantly affects the outcome of pregnancy .In most cases, the diagnosis is made based on clinical complaints and traditional methods. Since there is no gold standard diagnostic method, a noninvasive, specific, and rapid diagnostic tool is needed to predict PPROM. New and interesting parameters have been proposed in recent years for improving the diagnosis of PPROM so as to make rational and safe use of available therapeutic strategies.

A prospective case-control study was performed in the department of obstetrics and gynaecology in Dayanand Medical College on 150 pregnant women between 28weeks to 36weeks 6days period of gestation. This study was conducted to determine the usefulness, reliability, and cut-off values of vaginal fluid urea and creatinine measurement in detecting PPROM and to make appropriate recommendations based on the study results.

In our study, we found that confirmed rupture of membranes occurred in the majority of women 48% in 26 to 30year old age group, 42% in the over 30year old group, and 10% in the under 25year old group. Women in age group of 26 to 30year old accounted for 54% of the suspected and 52% of the control group. This is because unfavorable obstetric outcomes are associated with advanced maternal age. In our study, the mean age of women with confirmed rupture of membranes was 31 years +/- 5.64 years, the mean age of women with suspected rupture of membranes was 30.40+/-4.47 years, and the mean age of the control group was 31.46+/-4.84 years. Since there was no statistically significant age difference between the three groups in our study, this shows the age of pregnant women has no direct association with PPROM. Similar to our study, a prospective cohort study by Damien Bouvier et al on PPROM risk factors and outcomes, in the study group with confirmed leakage, the mean age

was 29.7+/- 4.7 years; in the group with suspected leakage, it was 29.3+/- 4.3 years; and in the control group, it was 30+/- 4.3 years. Among the three groups, there was no statistically significant difference. However, similar to our study, the majority of patients with confirmed leakage were between the ages of 26 and 30 years.[75] In contrast to our study, Berkowitz et al found that mothers who were 30 years of age or older had a noticeably higher risk of PPROM in their study on risk factors for preterm birth.[24] Heny Ekawati et al discovered that maternal ages at the extremes less than 25 years & more than 40 years are risk factors for preterm prelabour membrane rupture in their study of Factors Related to Prelabour Rupture of Membrane.[96] Ferguson et al made an observation regarding maternal age, found that the majority of PPROM cases occurred at extremes of maternal age 33.33% were less than 25 years old and 16.67% were older than 36 years.[25] In a systematic review of several well-designed, primarily retrospective cohort studies, Goldenberg et al (2008) concluded that maternal age was not a reliable indicator of preterm PROM.[13]

In our study, 70% of women with confirmed leakage, 52% in the suspected leakage group, and 72% in the control group were graduates. Women with confirmed leakage 4%, the suspected leakage group 6%, and 0% in the control group had a postgraduate degree. Women with confirmed leakage 8%, women with suspected leakage 8%, and 8% of women in the control group had an elementary school degree. Women with confirmed leakage 18%, 34% of patients with suspected leakage, and 20% of patients in the control group had secondary education. Our institute is a private tertiary care hospital, and the majority of women attending antenatal clinics are educated. In support of our study B.H. Jena et al. found an increased incidence of PPROM in women with primary education levels, but there was no statistically significant difference between primary and higher education levels with [p-value-0.76].[97] This is in contrast to our study Soheir Mahmoud Abd El-Hamid et al found that

low education was a significant risk factor for PPROM in a prospective cohort study of the relationship between preterm rupture of membranes and maternal and neonatal outcomes [98] Low education levels may be related to the likelihood of inappropriate utilization of prenatal care.

In our study, 62% of women with confirmed leakage, 40% of the suspect group, and 52% of the control group were working women. Women with confirmed leakage 38%, 60% with suspected leakage, and 48% of the control group were homemaker. In our study, working women have a higher incidence of preterm prelabour rupture of membranes, but there was no statistical significant difference between working women and homemaker (p-value 0.294). Similar to our study B.H. Jena et al in their prospective cohort study found that there was no statistical difference between the 2 groups' p-value of -0.24. [97] There have been limited studies on the association between PPROM and occupation.

In our study, the majority of women (38%) with confirmed leakage, 42% with suspected leakage, and 38% in the control group were from a lower-middle-class family. 32% of women with confirmed leakage, 38% of women with suspected leakage, and 24% in the control group were from upper-middle-class families. Women with confirmed leakage 12%, 2% of women with suspected leakage, and 8% of the control group were from an upper lower-class family. In confirmed leakage 0% women, suspected leakage 6% of women, and 2% of the control group were from a lower-class families. In 3 groups 18% of confirmed leakage, 12% of suspected leakage, and 28% of the control group were from an upper-class family. In our study, there was no statistically significant difference between the PPROM and control groups in terms of socioeconomic status. Similar results were also obtained by Polzin and Brady et al who found that the frequency of PPROM was negatively correlated with socioeconomic level·[37] Ortiz et al also found no statistically significant association between women's socioeconomic status and the risk of PROM. [99] In the

study, by Arnildo et al a higher rate of PPROM was found in women with lower socioeconomic status and lower educational level. In women from a lower socioeconomic class, the quality of prenatal examination is poor, with fewer consultations and fewer laboratory tests, which may be a causative factor in the occurrence of PPROM.[100] Noor et al in an observational study, found that PPROM was more common in women from the lower socioeconomic class. [101]

In our study, 90% of pregnancies with confirmed leakage, 94% with suspected leakage, and 86% in the control group were booked. 10% of pregnancies with confirmed leakage, 6% with suspected leakage, and 14% in the control group were unbooked. In our study, there was no statistically significant difference in all groups with a p value of 0.411. This can be explained by the fact that our institute is a private tertiary care hospital where patients are booked and the overall percentage of unbooked patients remains very low throughout the year. As per Government of India norms, every pregnant woman should have atleast 4 visits for antenatal checkup. Even one antenatal visit was associated with a reduction in the probability of neonatal mortality and reduction in probability of infant mortality.[102] These findings are at odds with a study by Sapna Chourasia et al who found that prenatal visits have large effects on maternal and fetal outcomes. [103] CH B Sridevi Geethanjali et al in their study found an association between PPROM and antenatal care and showed that 38% of women were booked cases, and 62% were non-booked cases, which is contradictory to our study. [104] In unbooked cases, there is a lack of antenatal care, which may fail to detect recurrent risk factors such as PPROM, preterm births, induced abortions and their treatment, and undetected urogenital infections.

In our study, most women were primigravida, 52% in the confirmed leakage group, 40% in the suspected leakage group, and 52% in the control group. In multigravida women, it was 48% with confirmed rupture

of membranes, 60% with suspected rupture of membranes, and 48% in the control group. Thus, in our study, most women with PPROM were primigravida. In support of our study, Shweta Somasikta Pani et al in their study found that the incidence of PPROM is higher in primigravida than in multigravida.[105] Estiyani Wulandari et al in their study on the correlation between parity and premature rupture of membranes 2013 found that the incidence of PPROM is higher in multigravida.[106] In primigravida, because the uterine wall does not change as much and the cervix does not experience frequent openings, it can support the membranes well . Women who had multiple births are at higher risk for PPROM because the vessels in the uterus are disrupted, leading to brittle membranes, fragile connective tissue, and eventually spontaneous rupture of the membranes.[107] No direct correlation between parity and PPROM has been found in other studies.

In our study majority of patients with confirmed leaking and the other two groups were with a period of gestation of more than 34 weeks and the rest with a period of gestation between 28 to 34 weeks. In support of our study; Shweta Somasikta Pani et al found in their study the incidence of PPROM more in women with a gestation age of more than 34 weeks.[105]

No patient had h/o pain abdomen in our study groups and control group. labor pain was an exclusion criterion in our study. In PPROM, most of the patients go into labour within a few hours. There is a release of fetal fibronectin by amnion epithelial cells. The fibronectin then binds to a specific toll-like receptor in the amnion mesenchymal cells and activates signaling cascades. These result in increased prostaglandin E synthesis (PGE2). Increased prostaglandin levels promote cervical ripening and uterine contractions. In a study by Biswas PR et al labour generally occurs within 24 hours of PPROM in 35-50%, within 72 hours in 70 %, and 90% deliver within two weeks.[108] American college of obstetrics and gynecology states that latency periods appear to be prolonged with

second-trimester PPROM as compared with PROM during later gestational ages. However, 40–50% of patients with periviable PROM give birth within the first week and approximately 70–80% gives birth within 2-5 weeks after membrane rupture. [109]

In our study, the mean duration of leakage on admission was less than 24 hours in both the group with confirmed leakage (13.28 hours) and the group with suspected leakage (16.83 hours), directly reflecting the awareness of patients to report to the hospital in case of leakage per vaginum. In a similar study conducted in the Department of Obstetrics and Gynecology, Lady Hardinge Medical College and Smt Sucheta Kriplani Hospital, New Delhi.[110] it was found that the mean duration of leakage before admission to the hospital was 22 hours, ranging from 8 to 38 hours.

In our study, it was seen on per speculum examination that in 100% of patients, in confirmed leaking the liquor was clear, watery in consistency and nonfoul smelling and on local examination pad was soaked with clear fluid in confirmed leaking. In suspected leaking pad was dry and clear in all patients. Meconium and blood-stained liquor were exclusion criteria in our study. The colour of amniotic fluid is clinically significant for deciding fetal prognosis as evidenced by a study conducted by Mazor et al.[111] Patients were classified according to the color of amniotic fluid into two groups: MSAF (meconium-stained amniotic fluid) and clear amniotic fluid. A higher rate of complications was noted in the MSAF group in comparison with patients with clear amniotic fluid [51% vs. 27.2%, respectively, p=0.003; 20% vs. 9.8%, respectively, p=0.0004]. According to ACOG,[1] Vaginal bleeding or blood-stained liquor should raise concern for abruptio placentae, which should prompt consideration of delivery, with the decision based on fetal status, the amount of bleeding, and gestational age.

Analysis of the results of urine cultures taken before antibiotics were administered showed that in 44% of patients, urine cultures were positive for the growth of microorganisms; in 56% of patients in the group with confirmed leakage, urine cultures were negative for the growth of microorganisms, in the group with suspected leakage, urine cultures were negative for growth in 94% and positive for growth in 6% of patients, in the control group, urine cultures were negative for growth in 90% and positive for growth in 10% of patients. UTI during pregnancy is significantly associated with the development of PPROM. In our study, there was no statistically significant difference between the urine cultures of the confirmed leak group with UTI and without UTI. Similar to our study a hospital-based study by Muhammad Nurhadi Rahman et al in their study found that PPROM were diagnosed with UTI has no statistically significant difference compared to patients PPROM with no UTI[112] Urinary tract infection in pregnancy is still one of the most common clinical problems in pregnancy. The condition is a serious problem for pregnant women. If left untreated, UTI can lead to pyelonephritis, preterm labor, or neonatal infections.[113] In contrast study by Singh et al[114], pregnant women with a history of UTI in pregnancy were 2.62 times more likely to have PPROM than those who did not have UTI.

Analysis of the results of vaginal culture taken before antibiotics were administered showed that in 46% of patients, the vaginal culture was positive for the growth of microorganisms, in 54% of patients the vaginal culture was negative for the growth of microorganisms in the group with confirmed leakage, in the group with suspected leakage 98% were negative for growth and 2% of patients had a positive vaginal culture for growth in control group 100% were negative for growth. Our study shows that Genital infections during pregnancy are significantly associated with the development of PPROM, as there was a statistically significant difference between patients in the group with confirmed leakage and the other two groups studied. The association between positive vaginal culture

in pregnancy and PPROM is also confirmed by studies by Kaye et al [115] in Uganda and Karat et al [116] in India. The association between PPROM and abnormal discharge, a common symptom of genital infections, is most likely due to inflammatory mediators [117]. In a study by Assefa et al[118] pregnant women with abnormal vaginal discharge had a 5.30-fold higher risk of PPROM than women who did not have abnormal vaginal discharge. This finding was consistent with the results of the study in Mekelle city, Ethiopia. However, a similar study[119] showed that the culture was positive in only 16% of women. The most common organism cultured was Escherichia coli 46.6%, followed by Klebsiella 33.3%, Pseudomonas 13.3%, and coagulase-negative Staphylococcus aureus 6.6%. These culture-positive patients were treated with antibiotics according to the results of the antibiotic susceptibility treatment.

In our study, 98% of patients in the confirmed leak group, 4% in the suspected leak group, and 0% in the no leak group had reduced AFI on ultrasound reports at admission. 1% of patients in the confirmed leak group, 48% in the suspected leak group, and 50% in the no leak group had AFI in the normal range (8-18 cm) on ultrasound at admission. The mean amniotic fluid index was 5.16 +/- 1.79 in the group with the confirmed leak, 12.88 +/- 3.56 in the group with the suspected leak, and 13.54 +/-3.01 in the control group. There is a statistically significant difference among the 3 groups studied. In support of our study, Weissmann-Brenner et al performed a retrospective study of pregnancies with complicated PPROM. The mean AFI in the PPROM and control groups was 5.8±3.6 cm (0-18.5 cm) and 13.7±3.2 cm (7.3-24.4 cm) (p value < 0.001).[120] The presence of a low AFI supports the diagnosis of PPROM. ROC Curve analysis revealed that an AFI ≤10 cm is the optimal cut-off value for suspicion of PPROM. An AFI of 10 cm had a sensitivity, specificity, positive predictive value, and negative predictive value of 89.2%, 88.5%, 72.2%, and 96%, respectively, to support the diagnosis of PPROM. Borna et al. reported that an AFI of 5 cm in PPROM patients

between 26 and 34 weeks of gestation increased the risk of maternal infection and cesarean delivery, which is consistent with the present study. [121] Singh D, Agarwal, et al in a comparative study in support of our study, found that the mean amniotic fluid index (AFI) was significantly lower in the case group than in the control group (5.3±1.7 vs. 11.3±1.5, $p < 0.001$). AFI was found to have a highly significant association between groups. (p value < 0.001). The sensitivity and specificity of the amniotic fluid index (AFI) for the diagnosis of PROM (case) were 97.5% and 92.5%, respectively, while the overall accuracy was 99.3%, with a cut-off value of ≤ 7.5 cm.[122] In patients with unremarkable leak and decreased AFI and suspected PROM. Ultrasonography for AFI may be the first screening examination performed to confirm vaginal leakage. However, there are other causes of decreased AFI or oligohydramnios, such as placental insufficiency, etc., so ultrasonography for AFI is not a method for definitive diagnosis of PPROM. In addition to ultrasonography for AFI, the determination of creatinine and urea values in the vaginal fluid may be useful in making a definitive diagnosis and planning appropriate treatment.

In our study, the mean urea content of vaginal fluid was 9.16+/-6.01 in the group with confirmed leakage and 2.06+/-0.82 in the group with suspected leakage, and 0.75+/-0.48 in the control group. The majority of patients had urea levels in the vaginal fluid between 5 and 25 in the group with confirmed leakage, and in the group with suspected leakage and the control group, most patients had urea levels in the vaginal fluid < 5. In our study, vaginal fluid urea levels were significantly higher than the control and suspected group with a p- value of 0.001. Vaginal fluid urea levels were higher in women with confirmed PPROM than in women with suspected PROM and in the control group. . Analysis of the ROC curve showed the vaginal fluid urea for the diagnosis of PPROM have a sensitivity of 98% for the confirmed leaking group, 82%% for suspected and specificity 100% for confirmed leaking group, 96% for suspects with a cut-off value of ≥2.5 mg/dl for cases and ≥1.5 for suspects.

Similar to our study Alao, A.I. Afolabi et al [2022] in their study on vaginal fluid urea and creatinine, an untapped diagnostic tool for premature rupture of membranes has found that vaginal fluid urea and creatinine are very effective tests in the diagnosis of PPROM. It is a cheaper and more readily available alternative to the Amnisure test. It is especially useful in our environment, especially in cases of equivocal PPROM, as a cost-effective means to confirm the diagnosis. Vaginal fluid urea and creatinine had sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV), respectively, of 94%, 82%, 93.18%, and 83.93%, and 98%, 90%, 97.82%, and 90.74%. The cutoff values for vaginal fluid urea and creatinine were 1.25 mg/dl and 0.23 mg/dl, respectively.[91] In support of our study Khaled M. Slama et al [123] a prospective case-control study conducted in the Department of Obstetrics and Gynaecology, Benha University Hospital, the mean vaginal fluid urea level in the PPROM group was 6.5 ± 2.48 mg/dl than in the control group at 3.4 ± 1.68 mg/dl, with a p value < 0.001. The ROC analysis showed that the best cut-off value was 3 mg/dl. The sensitivity, specificity, PPV, and NPV of vaginal fluid wash urea were 100%, 80%, 83.3%, and 100%, respectively.

Begum J et al [124] found that there was a statistically significant difference between the two groups in terms of vaginal fluid urea, with the mean value of urea in the study group being higher than in the control group (12.60 ± 4.85 vs. 2.12 ± 1.31, p-value < 0.001). The sensitivity and specificity of vaginal fluid urea for the diagnosis of PPROM were 98% and 100%, respectively. The PPV, NPV, and overall accuracy were 100%, 98.4%, and 99%, respectively, with a cut-off value > 6 mg/dl. Hesham M. et al. [125] performed a diagnostic study to evaluate and compare the reliability, accuracy, and cost-effectiveness of urea, creatinine, Beta-human chorionic gonadotropin (β-HCG), and placental alpha-microglobulin-1 (PAMG-1) in vaginal fluid for the diagnosis of premature rupture of the membranes, they found that the mean urea of vaginal fluid in the confirmed, suspicious, and control groups was 20.32 ± 5.6, 7.41 ± 4.02,

and 2.6 ± 3.06, respectively. Sensitivity, specificity, PPV, NPV, and accuracy of urea in the vaginal fluid were 96%, 95%, 96%, 95%, and 95.56%, respectively, at a cut-off value of > 4 mg/dl. There was a statistically significant difference between the studied groups in vaginal fluid urea p- value < 0.001.

In the study by Mohamed et al [84'], which enrolled 298 women and divided them into 3 groups (122 with confirmed ruptured membranes, 96 with suspected but not confirmed ruptured membranes, and 80 with intact membranes), the cut-off value for creatinine was (0.3 mg/dl) and for urea was (13 mg/dl) [35]. Shweta Somasikta PaniIn et al[105] in their study Role of vaginal fluid urea and creatinine in the diagnosis of preterm prelabour rupture of membrane found that the cut-off point of urea levels in vaginal fluid for final diagnosis of PPROM is 8 mg/dl. The urea value has a sensitivity of 93.3% and a specificity of 100%. Hasan Kafali et al in a similar study on vaginal fluid urea and creatinine levels in the diagnosis of premature rupture of membranes found that the mean vaginal fluid urea values in groups I, II, and III were 34.6 ± 5.3, 2.4 ± 5.3, and 1.3 ± 6.2 mg/dl, respectively, and the difference was statistically significant (P value< 0.001). [83]. Omneya M. Osman et al.[85] found in a prospective study conducted on 150 pregnant women in the third trimester (28-40 weeks) that the mean vaginal fluid urea concentration in the confirmed group was 1.87 mg/dl, which was higher than in the suspected group 0.32 mg/dl and the control group 0.11 mg/dl (p value< 0.05). The sensitivity, specificity, PPV, NPV, and accuracy of urea were all 100% at a cutoff value of 0.41 mg/dl. There was a statistically significant difference in urea levels between the confirmed, suspect, and control groups. The cut-off value for the detection of urea was > 0.41 mg/dl. Sensitivity, specificity, PPV, NPV, and accuracy were all 100%. There was an increase in creatinine and urea levels with increasing gestational age (r = 0.43 and 0.51, respectively, p value< 0.05). Cenk Gezer et al [86] in a prospective study of 100 pregnant women with PPROM and 100 healthy pregnant

women between 24 + 0 and 36 + 6 weeks gestation, found that the optimal cutoff values for the diagnosis of PPROM were > 6.7 mg/dl for urea and > 0.12 mg/dl for creatinine. In their study, Fatemeh Malchi et al found that the mean value of urea and creatinine was significantly higher in the case group than in the control group (MD=12.63,95%, CI[12.01,13.25])and(MD=0.31,95%, CI[0.29,0.32])[126]

In our study, the mean vaginal fluid creatinine value was 0.52 +/- 0.47 mg/dl in the group with confirmed leakage and 0.13 +/- 0.08 mg/dl in the group with suspected leakage, and 0.18 +/- 0.23 mg/dl in the control group. The majority of patients had creatinine values in the vaginal fluid between 0.2 mg/dl and 0.9 mg/dl in the group with confirmed leakage, ≤ 0.1 in the group with suspected leakage, and in the control group. In our study, vaginal fluid creatinine levels were in confirmed leaking group was significantly higher than the control and suspect groups with a p- value of 0.001. Analysis of the ROC curve showed the vaginal fluid creatinine for the diagnosis of PPROM has sensitivity of 88% for the confirmed leaking group, 46% for suspected, and specificity of 80% for the confirmed leaking group, 60% for suspects. of vaginal fluid creatinine for the diagnosis of PPROM with a cut-off value of ≥ 0.2 mg/dl for the confirmed leaking group and ≤ 0.1 for suspects. So by adding vaginal fluid creatinine, which is one of the diagnostic tests for PPROM, we can increase the sensitivity and specificity for the diagnosis of PPROM. Vaginal fluid creatinine is a rapid, simple, inexpensive, noninvasive, and widely available test, so it can be easily incorporated into routine clinical practice. Cenk Gezer et al [86] in a study on the diagnosis of preterm prelabour rupture of membranes and delivery interval after rupture of membranes, determined the optimal cutoff values for the diagnosis of PPROM based on urea and creatinine values vaginal fluid > 0.12 mg/dl for creatinine.

Similar study by Veena Ramasamy et al in their study found that the optimal cut-off value of vaginal fluid creatinine to detect ROM arrived

based on ROC curve analysis was ≥0.3 mg/dL. The mean vaginal fluid creatinine in group I was 1.097 mg/dL, in group II was 0.3 mg/dL, and in group III was 0.068 mg/dL. This study demonstrates that vaginal fluid creatinine could accurately diagnose a ROM with a sensitivity, specificity, positive predictive value, and negative predictive value of 98.36, 100, 100, and 97.14%, respectively[94]

G.B. Madhavi et al [127], in a prospective case-control study of vaginal fluid creatinine levels for the diagnosis of preterm prelabour rupture of the membranes, found that 97% of women in the control group had vaginal fluid creatinine levels of 0.3-0.6 mg/dl, whereas 1% of women with PPROM had the same level. In the control group 3% has > 0.3-0.6mg/dl creatinine levels in vaginal fluid, while 42% of women with PPROM have the same levels. Women in the control group 0% and 45% of women with PPROM have creatinine levels in vaginal fluid in the range of > 0.6-0.9mg/dl and 0% of women in the control group, 12% of women with PPROM have creatinine levels in vaginal fluid > 0.9mg/dl. They noted that the accuracy of vaginal fluid creatinine with a cutoff value of > 0.4mg/dl for diagnosing PPROM is more than 90%. The sensitivity, specificity, Positive predictive value, Negative predictive value, and accuracy of vaginal fluid creatinine to diagnose PROM were 99.89%,100.00%,100%, and 95.99% respectively with a cut-off value of >0.3.

Gürbüz et al. [93] compared the vaginal flushing fluid creatinine levels of 54 pregnant women in whom amnion flow was detected through speculum examinations with the creatinine levels of 34 pregnant women with no complaint. As a result, when the creatinine threshold was taken as 0.12 mg/dl, they observed sensitivity, specificity, and positive and negative predictive values to be 100%.a similar study conducted by Li Hy et al. [92] found that hCG, AFP, and creatinine concentrations were high in amniotic fluid. They reported that the assessment of hCG, AFP, and creatinine in vaginal flushing fluid was useful. They also stated that creatinine

assessment in vaginal flushing fluid is cheaper and easier than hCG and AFP in PPROM diagnosis

According to Ismail T. EL -Garhy et al (2019) in their study on the detection of creatinine in vaginal fluid for diagnosis of PPROM, the mean creatinine levels in vaginal fluid in the group (I) & group (II) were 0.70 ± 0.88 and 0.04 ± 0.18 mIU/mL respectively. The difference was statistically significant (p-value <0.001). At a creatinine cut-off value of 0.25 mIU/ml, the sensitivity and specificity for confirmation of PPROM were 72% and 94%, respectively[128]. Similar results were found in the study conducted by Zanjani and Haghighil [87]. The mean vaginal fluid creatinine levels in the group with confirmed PPROM, the group with suspected PROM, and the control group PPROM were 1.74 ± 0.8 mg/dl, 0.45 ± 0.2, and 0.25 ± 0.1 mg/dl, respectively. The difference was statistically significant (p-value < 0.001) In a recent cross-sectional study by Kuruoğlu et al (2019), a statistically significant difference was found between the creatinine levels of vaginal lavage fluid of PROM and non-PPROM patients. They found the mean creatinine level in vaginal flushing fluid was 0.39 (0.31) mg/dl in the PROM group, and 0.04 (0.10) mg/dl in the non-PROM group.[129]

SUMMARY AND CONCLUSION

This prospective study was conducted on 150 pregnant women between 28 weeks to 36 weeks 6 Days period of gestation presenting with preterm pre–labour rupture of membranes in the department of obstetrics and gynaecology at Dayanand Medical College and Hospital, Ludhiana to determine the diagnostic accuracy of vaginal washing fluid urea and creatinine in the detection of preterm pre-labour rupture of membranes.

- The mean age of patients presenting with PPROM was 31 years with a range of 22 to 41 years. It was found that the majority of cases of PPROM occurred at the extreme age of the mother in patients younger than 25 years (10%) and in patients older than 30 years (42%). However, no significant difference was found overall.
- The majority of female patients were educated and booked. It was found that as the education level of the patients decreased, the gestational age at presentation of PPROM also decreased, and this difference was found to be statistically significant in many studies.
- In our study, most women (62%) with confirmed leakage were employed. thirty-eight percent of women with confirmed leakage were homemaker. In our study, working women have a higher incidence of preterm prelabour rupture of membranes, but there was no significant statistical difference among 3 study groups between working women and homemaker.
- Majority of patients (52%) were primigravida but it was not directly related to PPROM.
- The majority of patients (34%) belonged to a lower-middle-class family. The difference in socioeconomic class proved to be statistically insignificant in our study.

- The mean duration of leakage at admission was less than 24 hours in both the confirmed leakage group (13.28 hours) and the suspected leakage group (16.83 hours). This is a direct indication that increased awareness in patients leads to early reporting to hospital in the event of PPROM.
- The majority of patients with leaking from all three groups had a gestation period of more than 34 weeks.
- On speculum examination, in 100% of patients with confirmed leakage had clear fluid, which was watery in consistency, and non foul-smelling. The colour of the amniotic fluid is clinically significant for deciding fetal prognosis.
- In our study,majority of patients belonging to group B and C had negative urine culture for growth of microorganisms. And this difference was statistically significant among three groups.
- In our study,majority of patients belonging to group B and C had negative vaginal culture for growth of microorganisms. And this difference was statistically significant among three groups.
- The mean amniotic fluid index was 5.16 +/- 1.79 in the group with confirmed leak, 12.88 +/- 3.56 in the group with suspected leak, and 13.54 +/-3.01 in the control group. There is a statistically significant difference among the 3 groups studied. Amniotic fluid index measurement at the time of admission is a valuable prognostic factor in the management of patients in addition to other diagnostic modalities.
- In our study, mean vaginal fluid urea levels were 9.16+/-6.01in the confirmed leaking group. Vaginal fluid urea value was higher in women with confirmed PPROM than in women with suspected PPROM and control group. Mean vaginal fluid creatinine levels 0.52 +/- 0.47 in confirmed leaking group. Vaginal fluid creatinine value was higher in women with confirmed PPROM than in other 2 groups. The optimum cut off

value for vaginal fluid urea in Group A and B was ≥2.5 mg/dl and ≥1.5 with sensitivity, specificity 98%, 100% and 82% ,96% respectively and cut off values for creatinine was≥ 0.2mg/dl and is ≥0.1 with sensitivity, specificity 88% ,80% and 46% ,60% respectively

Based on all the findings of our study we conclude that urea and creatinine in the vaginal fluid are reliable markers for the diagnosis of PPROM. Urea is a better predictor with high sensitivity and specificity. Both markers can be used in routine screening in addition to ultrasound for initiating timely obstetric intervention. These are the cheap as cost of these markers is 3 to 4 times less than other biochemical markers in the vaginal fluid. They are easily available alternative to current tests and cost wise, a big help in a developing country like ours.

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Sr. No	NAME	AGE(YR)	HUSBAND NAME	MRD NO	EDUCATION	OCCUPATION	MARRIED SINCE(YEAR)	SOCIOECONOMIC STATUS	RELATIONSHIP STATUS	BOOKED /UNBOOKED	MENSTURAL HISTORY				C
											LMP	EDOD	POG	OBSTETRICS FORMULA	present /suspect /absent
1	KM	38	RK	1209606	GRADUATE	HOUSEWIFE	2	UPPER MIDDLE CLASS	MARRIED	BOOKED	19-3-21	24-12-21	35WKS6DAYS	G1	S
2	MK	33	NS	1140556	SECONDARY	HOUSEWIFE	6	UPPER MIDDLE CLASS	MARRIED	BOOKED	8-3-21	13-12-21	36WKS6DAYS	G2P1L1	S
3	RR	40	RK	810216	SECONDARY	HOUSEWIFE	10	UPPER MIDDLE CLASS	MARRIED	BOOKED	10-3-21	15-12-21	36WKS5DAYS	G4P1L1A2	S
4	JK	40	JS	1191001	GRADUATE	GOVT JOB	5	UPPER CLASS	MARRIED	BOOKED	13-3-21	18-12-21	36WKS1DAY	G3P1L1A1	S
5	Lp	35	AK	788064	SECONDARY	HOUSEWIFE	6	UPPER MIDDLE CLASS	MARRIED	BOOKED	8-3-21	13-12-21	36WKS6DAYS	G2P1L1	S
6	Rk	30	TS	827322	PRIMARY	HOUSEWIFE	3	LOWER CLASS	MARRIED	BOOKED	8-3-21	13-12-21	36WKS6DAYS	G2A1	S
7	Sv	35	RK	1210414	GRADUATE	HOUSEWIFE	4	UPPER CLASS	MARRIED	UNBOOKED	14-3-21	19-12-21	36WKS	G2P1L1	S
8	MS	32	PS	1214397	SECONDARY	HOUSEWIFE	8	LOWER MIDDLE CLASS	MARRIED	BOOKED	8-5-21	15-2-22	28WKS6DAYS	G1	S
9	RK	30	KK	882445	SECONDARY	HOUSEWIFE	5	LOWER MIDDLE CLASS	MARRIED	BOOKED	20-4-21	27-1-22	35WKS4DAYS	G2P1L0	S
10	AK	26	SS	688764	GRADUATE	HOUSEWIFE	1	UPPER MIDDLE CLASS	MARRIED	BOOKED	13-4-21	20-1-22	36WKS4DAYS	G1	S
11	SD	32	SS	592052	GRADUATE	PVT JOB	5	LOWERMIDDLE CLASS	MARRIED	BOOKED	19-3-21	24-12-21	35WKS6DAYS	G1	P
12	PK	30	KK	1243682	GRADUATE	GOVT JOB	1	LOWER MIDDLE CLASS	MARRIED	BOOKED	4-6-21	11-3-22	33WKS2DAYS	G1	P
13	RV	28	G	980240	GRADUATE	PVT JOB	2	UPPERMIDDLE CLASS	MARRIED	BOOKED	5/5/21	12-2-21	31W1DAY	G1	P
14	R	47	TR	1221207	PRIMARY	HOUSEWIFE	18	UPPER MIDDLE CLASS	MARRIED	UNBOOKED	12-4-21	19-1-22	34WKS4DAY	G2P1LO	P
15	A	30	NS	1218251	GRADUATE	GOVT JOB	1	UPPER CLASS	MARRIED	BOOKED	05-08-2021	15/2/22	30WKS6DAYS	G1	P
16	G	35	SS	9043	GRADUATE	PVT JOB	4	LOWER MIDDLE CLASS	MARRIED	BOOKED	17/3/21	22/12/21	35WKS 6DAYS	G2P1L1	P
17	M	31	GS	4687	GRADUATE	PVT JOB	1	UPPER CLASS	MARRIED	BOOKED	03-08-2021	13/12/21	36WKS6DAYS	G1	P
18	N	30	LS	1211797	GRADUATE	GOVT JOB	2	UPPER MIDDLE CLASS	MARRIED	UNBOOKED	14/3/21	19/1/21	36WKS1DAY	G1	A
19	N	24	HK	893753	GRADUATE	HOUSEWIFE	2	LOWER MIDDLE CLASS	MARRIED	BOOKED	18/3/21	25/12/21	36WKS4DAYS	G2A1	A

CHIEF COMPLAINT				OBSTETRICS HISTORY	GENRAL EXAMINATION			INSPECTION	PER ABDOMEN				AUSCULTATION	LOCAL EXAMINATIONLLEAKING(+/ -)
LEAKING			GROUP A/B/C	(PRIMIGRAVIDA/ MULTIGRAVIDA)	BP	PULSE	TEMP		FH	Fetal lie	Presentation	Amniotic fluid NORMAL/DECREASED)	FHR(bpm)	
Duration(HOURS)	colour	Labour pains												
NA	NA	NO	B	PRIMI	110/70	82	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	126	-
NA	NA	NO	B	MULTI	110/70	86	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	146	-
NA	NA	NO	B	MULTI	120/70	74	NORMAL	LINEA NIGRA +, STRIA + TRANSEVESE SCAR +	34-36	LONG	CEPHALIC	NORMAL	156	-
NA	NA	NO	B	MULTI	110/60	98	NORMAL	LINEA NIGRA +, STRIA + TRANSEVESE SCAR +	34- 36	LONG	CEPHALIC	NORMAL	156	-
NA	NA	NO	B	MULTI	120/80	76	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	136	-
NA	NA	NO	B	MULTI	110/60	56	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	146	-
NA	NA	NO	B	MULTI	150/90	50	NORMAL	LINEA NIGRA +, STRIA +	34-36	TRANSEVERSE	TRASVERSE	NORMAL	130	-
NA	NA	NO	B	PRIMI	126/76	62	NORMAL	LINEA NIGRA +, STRIA +	28-30	LONG	CEPHALIC	NORMAL	152	-
NA	NA	NO	B	MULTI	110/72	96	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	147	-
NA	NA	NO	B	PRIMI	120/80	86	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	146	-
3	CLEAR	NO	A	PRIMI	110/60	74	NORMAL	LINEA NIGRA +, STRIA +	32-34	LONG	BREECH	DECREASED	153	+
6	CLEAR	NO	A	PRIMI	100/60	76	NORMAL	LINEA NIGRA +, STRIA +	30-32	LONG	BREECH	DECREASED	152	+
24	CLEAR	NO	A	PRIMI	110/70	82	NORMAL	LINEA NIGRA +, STRIA +	32-34	LONG	CEPHALIC	DECREASED	146	+
5	CLEAR	NO	A	MULTI	120/80	86	NORMAL	LINEA NIGRA +, STRIA + TRANSEVESE SCAR +	34-36	LONG	CEPHALIC	DECREASED	156	+
1	CLEAR	NO	A	PRIMI	100/60	92	NORMAL	LINEA NIGRA +, STRIA +	30-32	LONG	CEPHALIC	DECREASED	146	+
12	CLEAR	NO	A	MULTI	120/90	90	NORMAL	LINEA NIGRA +, STRIA + TRANSEVESE SCAR +	34-36	LONG	BREECH	DECREASED	146	+
4	CLEAR	NO	A	PRIMI	110/70	92	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	DECREASED	128	+
NA	NA	NO	C	PRIMI	110/90	82	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	126	-
NA	NA	NO	C	MULTI	110/80	74	NORMAL	LINEA NIGRA +, STRIA + TRANSEVESE SCAR +	34-36	LONG	CEPHALIC	NORMAL	148	-

VULVAL PAD ABSENT(A)/DRY(D)/WET(W)	PER SPECULUM POOLING (+/-)	INVESTIGATION				VAGINAL FLUID		HIGH	URINE
		HB	PLT	TLC	USG FWB (AMNIOTIC FLUID INDEX)	UREA	CREATININE	GROWTH(+ / -)	GROWTH (+/-)
A	-	10.9	253	17	10	3	0.15	-	GROWTH -
A	-	11	140	12	6	2	0.16	-	GROWTH -
A	-	8.6	200	13	18	2	0.17	-	GROWTH -
A	-	11	190	11	14	3	0.17	-	GROWTH -
A	-	9.6	200	10	7	2	0.17	-	GROWTH -
A	-	10	150	7	9	2	0.15	-	GROWTH -
A	-	9.6	162	5	10	3	0.17	-	GROWTH -
A	-	9	190	9	7	2	0.1	-	GROWTH +
A	-	10	194	6	14	3	0.12	-	GROWTH -
A	-	13	200	7	16	2	0.28	-	GROWTH-
W	+	10	100	17	5	8	0.59	+	GROWTH+
W	+	12	170	10	4	4	0.1	-	GROWTH+
W	+	10	180	7	2	22	0.89	+	GROWTH-
W	+	12	190	6	7	23	0.91	+	GROWTH +
W	+	8.9	150	4.6	3	27	1.6	-	GROWTH -
W	+	14	256	9	1	14	0.7	-	GROWTH -
W	+	12	300	7	7	10	0.6	+	GROWTH -
A	-	10	180	6	16	1	0.1	-	GROWTH -
A	-	12	180	7.8	14	0	0.1	-	GROWTH -

20	R	30	PS	124692	GRADUATE	PVT JOB	2	UPPER CLASS	MARRIED	BOOKED	14/3/21	19/12/21	36WKS4DAYS	G1	A
21	A	26	BS	1213331	GRADUATE	HOUSEWIFE	1	UPPER CLASS	MARRIED	BOOKED	17/3/21	22/12/21	35WKS6DAYS	G1	A
22	IB	29	LS	882245	GRADUATE	HOUSEWIFE	4	UPPER CLASS	MARRIED	BOOKED	14/3/21	19/12/21	36WKS4DAYS	G1	A
23	P	37	SS	7496	GRADUATE	GOVT JOB	6	LOWER MIDDLE	MARRIED	BOOKED	21/3/21	26/12/21	35WKS4DAYS	G1	A
24	DM	27	FS	1226235	GRADUATE	PVT JOB	2	LOWER MIDDLE	MARRIED	BOOKED	20/4/21	27/1/22	34WKS4DAY	G1	A
25	S	27	RJ	1218036	GRADUATE	HOUSEWIFE	4	UPPER MIDDLE CLASS	MARRIED	UNBOOKED	26/4/21	02-02-2021	35WKS4DAYS	G1	A
26	S	30	MS	1213282	PRIMARY	HOUSEWIFE	1	LOWER MIDDLE	MARRIED	BOOKED	20/3/21	23/1/21	36WKS2DAYS	G1	A
27	S	30	KD	911051	SECONDARY	HOUSEWIFE	2	LOWER MIDDLE	MARRIED	BOOKED	14/3/21	19/1/21	36WKS1DAY	G1A1	A
28	MK	33	AK	452463	PRIMARY	HOUSEWIFE	5	UPPER MIDDLE CLASS	MARRIED	B0OKED	28/5/21	03-07-2022	34WKS4DAY	G2P1L1A1	A
29	M	35	PS	1241773	SECONDARY	HOUSEWIFE	14	UPPER MIDDLE CLASS	MARRIED	BOOKED	15/5/21	19/2/22	36WKS1DAY	G5P2L1A2	A
30	DM	36	VM	1243308	SECONDARY	HOUSEWIFE	1	UPPER CLASS	MARRIED	BOOKED	29/5/21	03-07-2022	34WKS5DAY	G2P1L1	A
31	SG	26	AG	113399	GRADUATE	PVT JOB	3	LOWER MIDDLE	MARRIED	BOOKED	06-05-2021	03-12-2022	33WKS4DAY	G2P1L0	A
32	M	36	GS	1248744	GRADUATE	GOVT JOB	5	UPPER CLASS	MARRIED	BOOKED	06-02-2021	03-09-2022	36WKS	G1	A
33	G	28	AJ	188324	GRADUATE	HOUSEWIFE	6	LOWER MIDDLE	MARRIED	UNBOOKED	31/5/21	03-07-2022	36WKS	G3P1L1A1	A
34	K	46	GS	1200135	GRADUATE	HOUSEWIFE	18	LOWER MIDDLE	MARRIED	BOOKED	07-05-2021	04-10-2022	29WKS1DAY	G1	A
35	VW	34	RK	1244711	GRADUATE	HOUSEWIFE	8	UPPER LOWER CLASS	MARRIED	BOOKED	14/6/21	21/3/22	32WKS3DAYS	G2E1	A
36	A	30	AS	229674	GRADUATE	PVT JOB	8	UPPER CLASS	MARRIED	BOOKED	16/5/21	20/2/22	36WKS 4DAYS	G2P1L1A1	A
37	D	30	DS	1242739	GRADUATE	GOVT JOB	1	UPPER LOWER CLASS	MARRIED	BOOKED	29/5/21	03-07-2022	35WKS	G1	A
38	S	36	AJ	1248219	GRADUATE	PVT JOB	10	UPPER MIDDLE CLASS	MARRIED	BOOKED	05-09-2021	16/2/22	32WKS2DAY	G1	A
39	H	36	LK	1131688	GRADUATE	GOVT JOB	1	LOWER MIDDLE	MARRIED	BOOKED	06-08-2021	15/3/22	35 WKS	G1	A
40	R	38	JS	654	GRADUATE	PVT JOB	1	UPPER CLASS	MARRIED	BOOKED	29/5/21	03-05-2022	36WKS1DAY	G1	A
41	S	25	LS	1247444	GRADUATE	GOVT JOB	2	LOWER MIDDLE	MARRIED	BOOKED	05-07-2021	14/2/22	32WKS 2DAYS	G2P1L0	A
42	R	27	SB	1247859	GRADUATE	PVT JOB	1	UPPER CLASS	MARRIED	BOOKED	31/5/21	03-07-2022	36WKS	G1	A
43	S	30	HK	1248241	GRADUATE	HOUSEWIFE	1	LOWER MIDDLE	MARRIED	BOOKED	06-01-2021	03-08-2022	36WKS	G1	A
44	N	38	kk	1244272	GRADUATE	PVT JOB	2	LOWER MIDDLE	MARRIED	UNOOKED	11/6/21	18/3/22	32wks	G1	A
45	A	30	PP	1482556	GRADUATE	PVT JOB	1	UPPERMIDDLE CLASS	MARRIED	BOOKED	31/9/21	06-07-2022	36WKS	G2P1L1	A
46	MA	37	KS	1296789	GRADUATE	HOUSEWIFE	5	LOWER MIDDLE	MARRIED	BOOKED	09-08-2021	15/6/22	36WKS 5DAYS	G2P1L1	A
47	A	32	M RA	877288	SECONDARY	HOUSEWIFE	4	LOWER MIDDLE	MARRIED	BOOKED	13/9/21	20/6/22	36WKS	G2P1L1A1	A
48	VM	30	RR	1236890	SECONDARY	HOUSEWIFE	1	LOWER MIDDLE	MARRIED	BOOKED	4/10/21	07-11-2022	34WKS	G1	A
49	T	35	KK	1362281	PRIMARY	HOUSEWIFE	6	UPPER MIDDLE CLASS	MARRIED	BOOKED	23/10/21	30/7/22	34WKS	G2P1L1	A
50	A	34	PK	1359838	GRADUATE	HOUSEWIFE	1	LOWER MIDDLE	MARRIED	UNBOOKED	22/11/21	28/8/22	36WKS	G1	A
51	U	32	KJ	592952	SECONDARY	HOUSEWIFE	2	UPPER MIDDLE CLASS	MARRIED	UNBOOKED	7/10/22	14/7/22	34WKS5DAYS	G1	P
52	S	28	VS	1222606	GRADUATE	HOUSEWIFE	1	UPPER MIDDLE CLASS	MARRIED	BOOKED	25/11/21	02-01-2021	35WKS	G1	P
53	J	27	BS	1167742	GRADUATE	HOUSEWIFE	1	LOWER MIDDLE	MARRIED	BOOKED	25/5/21	25/2/22	34WKS 3DAYS	G1	P
54	T	23	RK	1248744	GRADUATE	HOUSEWIFE	2	UPPER LOWER CLASS	MARRIED	BOOKED	06-02-2021	03-09-2022	36WKS	G1	P
55	p	32	LK	9243811	GRADUATE	HOUSEWIFE	9	LOWER MIDDLE	MARRIED	BOOKED	27/6/21	04-03-2022	30WKS2DAYS	G3P1L1A1	P
56	k	32	sS	1154359	GRADUATE	PVT JOB	11	UPPER MIDDLE CLASS	MARRIED	BOOKED	14/6/22	14/3/22	33WKS	g3p2l2	P
57	y	30	NK	23272	GRADUATE	GOVT JOB	3	UPPER LOWER CLASS	married	BOOKED	14/4/21	21/1/22	32WKS	G2P1L1	P
58	p	25	kS	1243682	GRADUATE	HOUSEWIFE	1	LOWER MIDDLE	MARRIED	BOOKED	06-04-2021	03-11-2022	33+2WKS	G1	P
59	p	44	Vd	1296778	GRADUATE	HOUSEWIFE	2	LOWER MIDDLE	MARRIED	BOKKED	12/9/21	19/6/22	36WKS1DAYS	G3P2L1	P

NA	NA	NO	C	PRIMI	100/60	76	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	162	-
NA	NA	NO	C	PRIMI	90/60	100	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	156	-
NA	NA	NO	C	PRIMI	110/70	82	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	148	-
NA	NA	NO	C	PRIMI	110/60	76	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	156	-
NA	NA	NO	C	PRIMI	100/60	95	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	152	-
NA	NA	NO	C	PRIMI	90/60	85	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	156	-
NA	NA	NO	C	PRIMI	110/70	72	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	148	-
NA	NA	NO	C	MULTI	130/90	53	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	158	-
NA	NA	NO	C	MULTI	140/80	76	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	146	-
NA	NA	NO	C	MULTI	120/70	94	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	BREECH	NORMAL	148	-
NA	NA	NO	C	MULTI	110/70	82	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	156	-
NA	NA	NO	C	MULTI	120/70	76	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	148	-
NA	NA	NO	C	PRIMI	130/80	72	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	146	-
NA	NA	NO	C	MULTI	110/80	86	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	148	-
NA	NA	NO	C	PRIMI	130/90	80	NORMAL	LINEA NIGRA +, STRIA +	30-32	LONG	CEPHALIC	NORMAL	156	-
NA	NA	NO	C	MULTI	110/60	76	NORMAL	LINEA NIGRA +, STRIA +	32-34	LONG	CEPHALIC	NORMAL	156	-
NA	NA	NO	C	MULTI	120/70	80	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	156	-
A	NA	NO	C	PRIMI	110/73	82	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	148	-
NA	NA	NO	C	PRIMI	110/70	96	NORMAL	LINEA NIGRA +, STRIA +	30-32	LONG	CEPHALIC	NORMAL	156	-
NA	NA	NO	C	PRIMI	130/70	68	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	146	-
NA	NA	NO	C	PRIMI	110/70	70	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	142	-
NA	NA	NO	C	MULTI	120/70	72	NORMAL	LINEA NIGRA +, STRIA +	32-34	LONG	CEPHALIC	NORMAL	156	-
NA	NA	NO	C	PRIMI	130/70	88	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	156	-
NA	NA	NO	C	PRIMI	110/70	78	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	158	-
NA	NA	NO	C	PRIMI	120/70	94	NORMAL	LINEA NIGRA +, STRIA +	30-32	LONG	CEPHALIC	NORMAL	158	-
NA	NA	NO	C	MULTI	110/70	90	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	140	-
NA	NA	NO	C	MULTI	110/70	80	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	146	-
NA	NA	NO	C	MULTI	110/80	76	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	148	-
NA	NA	NO	C	PRIMI	110/81	76	NORMAL	LINEA NIGRA +, STRIA +	34-36	LONG	CEPHALIC	NORMAL	158	-
NA	NA	NO	C	MULTI	110/82	76	NORMAL	LINEA NIGRA + ,STRIA+	34-36	LONG	CEPHALIC	NORMAL	162	-
NA	NA	NO	C	PRIMI	110/83	76	NORMAL	LINEA NIGRA+, STRIA +	34-36	LONG	CEPHALIC	NORMAL	146	-
2	CLEAR	no	A	PRIMI	120/70	82	NORMAL	LINEA NIGRA+, STRIA +	32-34	LONG	CEPHALIC	DECREASED	146	+
12	CLEAR	NO	A	PRIMI	110/70	80	NORMAL	LINEANIGRA+,STRIA+	34-36	LONG	BREECH	DECREASED	156	+
12	CLEAR	no	A	PRIMI	120/80	70	NORMAL	LINEA NIGRA+, STRIA +	34-36	LONG	CEPHALIC	DECREASED	156	+
2	CLEAR	NO	A	PRIMI	110/76	60	NORMAL	LINEA NIGRA+, STRIA +	34-36	LONG	CEPHALIC	DECREASED	146	+
72	CLEAR	NO	A	MULTI	120/80	76	NORMAL	LINEA NIGRA+ ,STRIA+	28-30	LONG	CEPHALIC	DECREASED	156	+
48	CLEAR	no	A	MULTI	130/90	98	NORMAL	LINEA NIGRA + ,STRIA + VERTICAL	32-34	TRANSEVERSE	TRASVERSE	DECREASED	136	+
3	CLEAR	NO	A	MULTI	120/70	86	NORMAL	LINEA NIGRA+, STRIA +	32-34	LONG	CEPHALIC	DECREASED	148	+
1	CLEAR	NO	A	PRIMI	110/70	68	NORMAL	LINEA NIGRA+ ,STRIA+	34-36	LONG	BREECH	DECREASED	148	+
2	CLEAR	NO	A	MULTI	120/70	98	NORMAL	LINEA NIGRA +,STRIA+	34-36	LONG	CEPHALIC	DECREASED	156	+

A	-	8.6	120	7.4	16	0	0.1	-	GROWTH -
A	-	12	500	17	18	1	0.1	-	GROWTH -
A	-	10.5	324	5.7	16	1	0.1	-	GROWTH -
A	-	13	200	2.3	16	1	0.1	-	GROWTH -
A	-	13	140	8	14	1	0.1	-	GROWTH +
A	-	11	222	4.7	17	1	0.09	-	GROWTH -
A	-	9.9	150	3.5	18	1	1	-	GROWTH -
A	-	12	156	4.3	15	1	1.8	-	GROWTH -
A	-	14	160	5.5	12	1	0.1	-	GROWTH -
A	-	11	154	8.9	14	1	0.1	-	GROWTH -
A	-	10	164	10.1	10	1	0.1	-	GROWTH -
A	-	8.9	120	12.6	12	1	0.19	-	GROWTH -
A	-	13..2	160	10.6	5	1	0.2	-	GROWTH +
A	-	12.1	8.9	120	7	0.2	0.13	-	GROWTH -
A	-	10	7.6	100	9	0.1	0.1	-	GROWTH -
A	-	9	6.9	254	10	1	0.19	-	GROWTH -
A	-	10.1	9	180	12	0	0.1	-	GROWTH -
A	-	13	7.8	140	14	1	0.1	-	GROWTH+
A	-	11	6	180	10	0.3	0.2	-	GROWTH -
A	-	12	5	200	13	0.1	0.18	-	GROWTH -
A	-	10	8	180	16	0.1	0.17	-	GROWTH -
A	-	9	8.5	200	14	0.1	0.17	-	GROWTH -
A	-	10	7	325	15	1	0.19	-	GROWTH -
A	-	11	5.6	400	7	1	0.19	-	GROWTH -
A	-	12	6	200	12	1	0.1	-	GROWTH -
A	-	10	7	160	10	0	0.1	-	GROWTH -
A	-	7.7	17.8	27	12	1	0.1	-	GROWTH -
A	-	9	12.3	156	10	2	0.1	-	GROWTH -
A	-	10	11	245	13	1	0.1	-	GROWTH -
A	-	11	10	345	14	0.3	0.1	-	GROWTH -
A	-	10	9	200	15	0.1	0.1	-	GROWTH -
W	+	9	10	148	5	14	0.88	+	GROWTH -
W	+	10	16	206	4	7	0.27	+	GROWTH +
W	+	12	10	205	1	6	0.71	-	GROWTH +
W	+	10	14	170	2	9	0.3	-	GROWTH -
W	+	8.6	20	444	5	13	0.68	-	GROWTH +
W	+	11.1	12.6	243	4	13	0.65	-	GROWTH -
W	+	12	10	180	4	4	0.15	+	GROWTH -
W	+	10	7	200	6	4	0.1	+	GROWTH +
W	+	12	8	190	9	9	0.3	+	GROWTH +

60	C	29	Dk	1230516	GRADUATE	PVT JOB	1	UPPER LOWER CLASS	MARRIED	BOOKED	09-04-2021	06-11-2022	36WKS	G1	P
61	S	31	ps	1267210	GRADUATE	PVT JOB	5	UPPER MIDDLE CLASS	MARRIED	UNBOOKED	30/10/21	08-06-2023	32WKS2DAYS	G2A1	P
62	ANU	30	Bs	1300152	GRADUATE	PVT JOB	3	LOWER MIDDLE	MARRIED	BOOKED	11/9/21	18/6/22	36WKS2DAYS	G1	P
63	MK	24	MS	1298963	GRADUATE	PVT JOB	2	UPPER CLASS	MARRIED	BOOKED	7/11/21	14/8/22	28WKS3DAYS	G1	P
64	GK	32	KS	536742	SECONDARY	PVT JOB	4	LOWER MIDDLE	MARRIED	BOOKED	08-09-2021	16/5/22	35WKS	G2P1L1	P
65	N	35	ML	3004	GRADUATE	GOVT JOB	8	UPPER MIDDLE CLASS	MARRIED	BOKKED	08-08-2021	15/5/22	36WKS	G3P1L1A1	P
66	RK	49	HS	124005	GRADUATE	PVT JOB	16	UPPER CLASS	MARRIED	BOOKED	19/7/21	26/4/22	31WKS 6DAYS	G4P1L0A2	P
67	S	30	PS	1263916	PRIMARY	PVT JOB	5	LOWER MIDDLE	MARRIED	UNBOKKED	09-08-2021	15/6/22	28WKS	G1	P
68	K	30	MK	1033139	GRADUATE	GOVT JOB	5	UPPER LOWER CLASS	MARRIED	BOOKED	07-05-2021	04-12-2022	35WKS	G1	P
69	TK	43	SS	1262085	GRADUATE	PVT JOB	4	UPPER MIDDLE CLASS	MARRIED	BOOKED	15/8/21	22/5/22	33WKS	G1	P
70	SK	41	JS	1260834	GRADUATE	PVT JOB	8	LOWER MIDDLE	MARRIED	BOOKED	29/7/21	05-05-2022	35WKS4DAYS	G3P1L1A1	P
71	RK	30	GS	1342910	GRADUATE	HOUSEWIFE	4	UPPER LOWER CLASS	MARRIED	BOOKED	27/7/21	05-02-2022	36WKS	G2A1	P
72	SA	26	LA	1239620	GRADUATE	HOUSEWIFE	4	UPPER MIDDLE CLASS	MARRIED	BOOKED	28/1/21	11-04-2022	29WKS	G1	P
73	RR	27	AK	382832	GRADUATE	GOVT JOB	4	UPPER MIDDLE CLASS	MARRIED	BOOKED	25/1/21	11-01-2022	29WKS3DAYS	G1	P
74	HK	34	HS	1285878	GRADUATE	PVT JOB	6	LOWER MIDDLE	MARRIED	BOOKED	14/12/21	21/9/22	36WKS	G2P1L1	P
75	MK	28	KS	136320	SECONDARY	HOUSEWIFE	2	LOWER MIDDLE	MARRIED	BOOKED	14/12/21	21/9/22	36WKS	G1	P
76	SR	24	JS	135876	SECONDARY	PVT JOB	4	UPPER LOWER CLASS	MARRIED	BOOKED	27/12/21	10-02-2022	30WKS	G4A3	P
77	AR	30	PK	1358878	POSTGRADUATE	HOUSEWIFE	5	UPPER CLASS	MARRIED	booked	2/12/21	09-09-2022	33WKS3DAYS	G1	P
78	AR	29	KS	1237762	SECONDARY	HOUSEWIFE	4	UPPER MIDDLE CLASS	MARRIED	BOOKED	24/11/21	31/8/22	36WKS6DAYS	G3P1L1A1	P
79	AK	27	MK	1358038	SECONDARY	GOVT JOB	6	UPPER CLASS	MARRIED	BOOKED	20/11/21	27/8/22	36WKS5DAY	G2P1L1	P
80	SA	27	SS	1116196	PRIMARY	HOUSEWIFE	2	LOWER MIDDLE	MARRIED	UNBOKKED	19/11/21	26/8/22	36WKS6DAYS	G2A1	P
81	DK	36	SS	1357136	SECONDARY	HOUSEWIFE	8	LOWER MIDDLE	MARRIED	BOOKED	26/11/21	09-01-2022	36WKS	G2P1L1	P
82	CK	34	BS	154702	GRADUATE	PVT JOB	7	UPPER CLASS	MARRIED	BOOKED	23/11/21	30/8/22	36WKS3DAYS	G3P2L2	P
83	AK	34	SS	436037	GRADUATE	GOVT JOB	6	UPPER MIDDLE CLASS	MARRIED	BOOKED	5/1/22	10-07-2022	35WKS	G1	P
84	SA	29	SA	1207500	SECONDARY	PVT JOB	4	LOWER MIDDLE	MARRIED	BOOKED	15/12/21	22/9/22	35WKS3DAYS	G1	P
85	AR	25	SK	1362228	GRADUATE	HOUSEWIFE	4	LOWER MIDDLE	MARRIED	BOOKED	12/12/21	17/9/22	35WS	G1	P
86	JJ	38	MS	1265879	GRADUATE	GOVT JOB	8	LOWER MIDDLE	MARRIED	BOOKED	9/12/21	16/9/22	36WKS	G2P1L1	P
87	N	30	RK	846909	SECONDARY	PVT JOB	4	UPPER MIDDLE CLASS	MARRIED	BOKKED	23/2/22	30/11/22	30WKS	G2A1	P
88	JK	37	YS	1240227	GRADUATE	PVT JOB	8	UPPER MIDDLE CLASS	MARRIED	BOOKED	09-07-2021	14/6/22	36WKS6DAYS	G2PIL1	P
89	RD	28	NK	796172	PRIMARY	GOVT JOB	7	UPPER MIDDLE CLASS	MARRIED	BOOKED	3/12/21	09-10-2022	32WKS	G1	P
90	H	27	KS	1415277	GRADUATE	GOVT JOB	3	UPPER CLASS	MARRIED	BOOKED	01-09-2022	16/10/22	32WKS	G2P1L1	P
91	GK	30	TS	1011631	GRADUATE	HOUSEWIFE	2	UPPER MIDDLE CLASS	MARRIED	BOOKED	17/12/21	24/9/22	35WKS	G2A1	P
92	NC	31	JS	1207135	GRADUATE	HOUSEWIFE	1	LOWER MIDDLE	MARRIED	BOOKED	10/12/21	17/9/22	36WKS	G1	P
93	J	29	SS	1277377	POSTGRADUATE	HOUSEWIFE	3	UPPER CLASS	MARRIED	BOOKED	21/10/21	28/7/22	32WKS	G1	P
94	H	30	KK	1216234	GRADUATE	PVT JOB	4	UPPER LOWER CLASS	MARRIED	UNBOOKED	05-04-2021	02-11-2022	36WKS	G2P1L1	A
95	KK	29	SK	146724	GRADUATE	GOVT JOB	2	UPPER CLASS	MARRIED	BOOKED	11/4/21	18/1/22	34WKS	G3A2	A
96	RR	30	RR	1345	GRADUATE	HOUSEWIFE	2	UPPER CLASS	MARRIED	BOOKED	13/5/21	20/2/22	34WKS5DAYS	G1A1	A
97	Bk	28	KK	1248299	GRADUATE	GOVT JOB	4	UPPER MIDDLE CLASS	MARRIED	BOOKED	17/4/21	24/1/22	35WKS	G1	S
98	B	27	SS	1241679	GRADUATE	PVT JOB	5	LOWER MIDDLE	MARRIED	BOOKED	11/4/21	18/1/22	36WKS	G1	S
99	RK	36	GS	1226126	GRADUATE	PVT JOB	2	UPPER CLASS	MARRIED	BOOKED	15/4/21	22/1/22	35WKS2DAYS	G1	S
100	N	29	KK	203328	GRADUATE	HOUSEWIFE	2	LOWER MIDDLE	MARRIED	BOOKED	14/4/21	21/1/22	35WKS	G2A1	S
101	DA	27	MA	1228649	POSTGRADUATE	PVT JOB	1	UPPER CLASS	MARRIED	BOOKED	23/4/21	24/12/21	35WKS	G2A1	S

2	CLEAR	NO	A	PRIMI	110/70	86	NORMAL	LINEA NIGRA ,STRIA +	34-36	LONG	BREECH	DECREASED	156	+
2	CLEAR	NO	A	MULTI	120/70	100	NORMAL	LINEA NIGRA+ ,STRIA+	30-32	LONG	CEPHALIC	DECREASED	163	+
3	CLEAR	NO	A	PRIMI	110/70	98	NORMAL	LINEA NIGRA+, STRIA +	34-36	LONG	CEPHALIC	NORMAL	146	+
24	CLEAR	NO	A	PRIMI	110/60	86	NORMAL	LINEA NIGRA+ ,STRIA+	28-30	LONG	CEPHALIC	DECREASED	156	+
6	CLEAR	NO	A	MULTI	150/90	76	NORMAL	LINEA NIGRA +,STRIA+ SCAR +	34-36	LONG	CEPHALIC	DECREASED	158	+
24	CLEAR	NO	A	MULTI	140/80	76	NORMAL	LINEA NIGRA+ ,STRIA+	34-36	LONG	CEPHALIC	DECREASED	162	+
3	CLEAR	NO	A	MULTI	120/70	72	NORMAL	LINEA NIGRA + ,STRIA +	30-32	LONG	BREECH	DECREASED	156	+
5	CLEAR	NO	A	PRIMI	130/90	76	NORMAL	LINEANIGRA+,STRIA+	20-30	LONG	CEPHALIC	DECREASED	146	+
2	CLEAR	NO	A	PRIMI	120/90	86	NORMAL	LINEA NIGRA+, STRIA +	34-36	LONG	CEPHALIC	DECREASED	120	+
3	CLEAR	NO	A	PRIMI	110/70	76	NORMAL	LINEA NIGRA+ ,STRIA+	32-34	LONG	BREECH	DECREASED	162	+
12	CLEAR	NO	A	MULTI	120/70	86	NORMAL	LINEA NIGRA + STRIA	34-36	LONG	CEPHALIC	DECREASED	148	+
4	CLEAR	NO	A	MULTI	110/70	98	NORMAL	LINEA NOGRA+ STRIA +	34-36	LONG	CEPHALIC	DECREASED	156	+
4	CLEAR	NO	A	PRIMI	140/90	100	NORMAL	LINEA NIGRA +,STRIA +	28-30	LONG	BREECH	DECREASED	148	+
5	CLEAR	NO	A	PRIMI	120/70	98	NORMAL	LINEA NIGRA+,STRIA+	28-30	LONG	CEPHALIC	DECREASED	156	+
6	CLEAR	NO	A	MULTI	110/70	102	NORMAL	LINEA NIGRA+,STRIA+,TRANSVERSE	34-36	LONG	CEPHALIC	DECREASED	148	+
4	CLEAR	NO	A	PRIMI	110/70	108	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	DECREASED	146	+
24	CLEAR	NO	A	MULTI	120/80	88	NORMAL	LINEA NIGRA+,STRIA+	28-30	LONG	CEPHALIC	DECREASED	148	+
9	CLEAR	NO	A	PRIMI	130/70	98	NORMAL	LINEA NIGRA+,STRIA+	32-34	LONG	BREECH	DECREASED	156	+
3	CLEAR	NO	A	MULTI	120/80	100	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	DECREASED	135	+
24	CLEAR	NO	A	MULTI	140/90	94	NORMAL	LINEA NIGRA+,STRIA+,TRANSVERSE	34-36	LONG	CEPHALIC	DECREASED	138	+
3	CLEAR	NO	A	MULTI	150/80	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	DECREASED	128	+
5	CLEAR	NO	A	MULTI	120/80	84	NORMAL	LINEA NIGRA+,STRIA+,TRANSVERSE	34-36	LONG	CEPHALIC	DECREASED	148	+
3	CLEAR	NO	A	MULTI	110/70	96	NORMAL	LINEA NIGRA+,STRIA+,TRANSVERSE	34-36	LONG	CEPHALIC	DECREASED	146	+
3	CLEAR	NO	A	PRIMI	130/80	94	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	DECREASED	145	+
24	CLEAR	NO	A	PRIMI	130/70	80	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	DECREASED	156	+
72	CLEAR	NO	A	PRIMI	150/80	96	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	DECREASED	126	+
48	CLEAR	NO	A	MULTI	110/70	88	NORMAL	LINEA NIGRA+,STRIA+,TRANSVERSE	34-36	LONG	CEPHALIC	DECREASED	156	+
24	CLEAR	NO	A	MULTI	120/70	78	NORMAL	LINEA NIGRA+,STRIA+	28-30	LONG	CEPHALIC	DECREASED	156	+
92	CLEAR	NO	A	MULTI	120/71	98	NORMAL	LINEA NIGRA+,STRIA+,TRANSVERSE	34-34	LONG	CEPHALIC	DECREASED	136	+
4	CLEAR	NO	A	PRIMI	120/72	86	NORMAL	LINEA NIGRA+,STRIA+	30-32	LONG	BREECH	DECREASED	145	+
2	CLEAR	NO	A	MULTI	120/73	86	NORMAL	LINEA NIGRA+,STRIA+	30-32	LONG	CEPHALIC	DECREASED	158	+
1	CLEAR	NO	A	MULTI	120/74	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	DECREASED	148	+
2	CLEAR	NO	A	PRIMI	120/75	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	DECREASED	156	+
3	CLEAR	NO	A	PRIMI	120/76	86	NORMAL	LINEA NIGRA+,STRIA+	30-32	LONG	CEPHALIC	DECREASED	136	+
NA	NA	NO	C	MULTI	120/77	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	134	-
NA	NA	NO	C	MULTI	120/78	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	156	-
NA	NA	NO	C	MULTI	120/79	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	145	-
1	CLEAR	NO	B	PRIMI	110/70	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	146	-
1	CLEAR	NO	B	PRIMI	120/80	98	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	148	-
3	CLEAR	NO	B	PRIMI	110/80	96	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	156	-
2	CLEAR	NO	B	MULTI	120/80	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	146	-
5	CLEAR	NO	B	MULTI	140/100	90	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	148	-

W	+	10	9	200	7	7	0.3	-	GROWTH +
W	+	10	13	423	5	4	0.2	+	GROWTH -
W	+	9	10	150	8	4	0.2	-	GROWTH -
W	+	10	20	140	7	4	0.2	-	GROWTH -
W	+	12	14	150	4	3	0.3	-	GROWTH +
W	+	10	12	106	5	12	0.2	-	GROWTH +
W	+	12	10	246	2	4	2.95	-	GROWTH -
W	+	10	10	300	4	7	0.2	+	GROWTH -
W	+	12	10	200	6	13	0.2	+	GROWTH +
W	+	12	6	150	6	4	0.2	+	GROWTH +
W	+	10	8	200	7	13	0.2	-	GROWTH +
W	-	10	7	405	7	12	0.3	-	GROWTH -
W	+	11	9	335	7	4	0.2	+	GROWTH -
W	+	12	8	230	5	12	0.9	+	GROWTH +
W	+	13	17	130	4	4	0.4	-	GROWTH -
W	+	12	10	206	4	2	1.04	+	GROWTH -
W	+	10	6	160	4	7	0.3	+	GROWTH -
W	+	9	8	180	6	4	0.4	-	GROWTH +
W	+	15	6	170	7	4	0.4	-	GROWTH -
W	+	10	9	230	7	4	0.49	-	GROWTH -
W	+	8.8	12	244	4	14	0.6	-	GROWTH +
W	+	9	15	140	5	8	0.31	-	GROWTH -
W	+	8.9	18	189	5	4	0.82	+	GROWTH +
W	+	11	5	96	7	4	0.3	+	GROWTH +
W	+	13	8	123	5	15	0.84	+	GROWTH -
W	+	10	3	345	4	27	0.6	+	GROWTH -
W	+	9.5	6	250	4	13	0.6	-	GROWTH -
W	+	7	7	190	7	4	0.44	+	GROWTH -
W	+	9.9	8	130	6	4	0.38	-	GROWTH -
W	+	10	9	120	6	10	0.8	-	GROWTH +
W	+	10	8	140	7	10	0.9	-	GROWTH -
W	+	10	9	158	5	10	0.1	+	GROWTH -
W	+	10	6	176	5	10	0.11		GROWTH +
W	+	10	12	230	7	10	0.12	-	GROWTH +
D	-	10	12	200	14	1	0.13	-	GROWTH -
D	-	10	10	160	10	1	0.14	-	GROWTH -
D	-	9.9	6	140	12	2	0.1	-	GROWTH -
D	-	8.9	7	180	13	2	0.2	-	GROWTH -
D	-	9	8	200	7	2	0.1	+	GROWTH -
D	-	14	8	356	14	2	0.1	-	GROWTH -
D	-	12	8	200	16	2	0.1	-	GROWTH -
D	-	10	7	140	17	2	0.14	-	GROWTH -

102	M	29	KS	1241707	GRADUATE	HOUSEWIFE	6	UPPER LOWER CLASS	MARRIED	BOOKED	05-09-2021	16/2/22	34WKS3DAYS	G5P2L0A2	S
103	NK	34	NS	103648	GRADUATE	PVT JOB	3	LOWER CLASS	MARRIED	BOOKED	06-06-2021	15/3/22	32wks5days	G4A3	S
104	SK	32	GS	1243290	GRADUATE	GOVT JOB	1	UPPER MIDDLE CLASS	MARRIED	BOOKED	19/6/21	26/3/22	31WKS1DAY	G1	S
105	NK	23	LS	1156661	GRADUATE	PVT JOB	1	LOWER MIDDLE	MARRIED	BOOKED	05-09-2021	16/2/22	36WKS2DAYS	G1	S
106	MS	26	MS	1168019	GRADUATE	PVT JOB	5	LOWER MIDDLE	MARRIED	BOOKED	05-09-2021	16/2/22	36WKS2DAYS	G2A1	S
107	DK	28	SK	1111697	GRADUATE	HOUSEWIFE	8	UPPER MIDDLE CLASS	MARRIED	BOOKED	25/11/21	09-01-2022	36WKS	G1	S
108	S	27	RK	929884	GRADUATE	HOUSEWIFE	8	LOWER MIDDLE	MARRIED	BOOKED	9/12/21	16/9/22	34WKS	G4A3	S
109	HK	28	JK	1233893	SECONDARY	HOUSEWIFE	4	LOWER CLASS	MARRIED	BOOKED	25/11/21	09-01-2022	36WKS	G1	S
110	JK	38	K	35656	SECONDARY	HOUSEWIFE	3	LOWER MIDDLE	MARRIED	BOOKED	20/5/21	27/2/22	35WKS6DAYS	G2P1L1	S
111	TK	28	M	1151834	GRADUATE	HOUSEWIFE	2	LOWER MIDDLE	MARRIED	BOOKED	22/4/21	29/1/22	34WKS5DAYS	G1	S
112	SK	29	GH	1222350	GRADUATE	PVT JOB	2	UPPER CLASS	MARRIED	BOOKED	26/5/21	03-05-2022	35WKS	G3P2L2	S
113	MK	30	HS	1284704	PRIMARY	GOVT JOB	1	UPPER MIDDLE CLASS	MARRIED	BOOKED	06-02-2021	03-09-2022	34WKS	G1	S
114	MK	24	TK	123756	SECONDARY	PVT JOB	2	LOWER MIDDLE	MARRIED	BOOKED	27/6/21	4/4/22	34WKS6DAYS	G6A5	S
115	R	28	SJ	1221207	PRIMARY	GOVT JOB	2	UPPER MIDDLE CLASS	MARRIED	BOOKED	05-05-2021	02-05-2022	36WKS	G1	S
116	K	30	JK	1033139	SECONDARY	HOUSEWIFE	6	LOWER MIDDLE	MARRIED	BOOKED	27/7/21	05-03-2022	32WKS	G2P1L1	S
117	S	41	JS	1260834	GRADUATE	HOUSEWIFE	6	LOWER MIDDLE	MARRIED	BOOKED	14/7/21	21/4/22	34WKS	G4P1L1A2	S
118	P	28	NN	1297889	GRADUATE	HOUSEWIFE	4	UPPER MIDDLE CLASS	MARRIED	BOOKED	28/10/21	07-04-2022	28WKS6DAYS	G2A1	S
119	D	35	NA	1297521	POSTGRADUATE	PVT JOB	8	UPPER MIDDLE CLASS	MARRIED	BOOKED	10/9/21	17/6/22	35WKS	G4P2L2A1	S
120	AK	32	MRA	877288	SECONDARY	HOUSEWIFE	14	LOWER MIDDLE CLASS	MARRIED	BOOKED	09-03-2021	10/6/22	36WKS	G3PIL1A1	S
121	M	37	KK	1296789	POSTGRADUATE	HOUSEWIFE	5	UPPER MIDDLE CLASS	MARRIED	BOOKED	29/8/21	06-05-2022	36WKS4DAYS	G2P1L1	S
122	A	28	HK	1261232	GRADUATE	PVT JOB	4	UPPER MIDDLE CLASS	MARRIED	UNBOOKED	15/8/21	22/5/22	30WKS	G3P2L2	S
123	M	30	RS	129863	GRADUATE	HOUSEWIFE	4	UPPER MIDDLE CLASS	MARRIED	BOOKED	2/11/21	9/8/22	28WKS3DAYS	G1	S
124	S	24	SK	1362512	GRADUATE	HOUSEWIFE	3	LOWER MIDDLE	MARRIED	BOOKED	11/6/21	18/3/22	34WKS	G1	S
125	R	30	GS	128697	GRADUATE	GOVT JOB	3	UPPER MIDDLE CLASS	MARRIED	BOOKED	28/6/21	03-07-2022	36WKS	G2A1	S
126	V	24	GK	1366914	GRADUATE	HOUSEWIFE	3	UPPER MIDDLE CLASS	MARRIED	BOOKED	16/1/21	23/10/22	32WKS	G1	S
127	N	30	JG	1014938	GRADUATE	HOUSEWIFE	1	UPPER MIDDLE CLASS	MARRIED	BOOKED	14/7/21	21/4/22	33WKS2DAYS	G2P1L1	S
128	SG	32	H	1364611	SECONDARY	PVT JOB	4	LOWER MIDDLE	MARRIED	BOOKED	29/12/21	5/9/22	34WKS1DAY	G4A3	S
129	JG	28	HD	1366914	SECONDARY	HOUSEWIFE	2	LOWER MIDDLE	MARRIED	UNBOOKED	01-05-2022	12/10/22	36WKS	G2P1L1	S
130	S	26	LS	1362759	GRADUATE	GOVT JOB	3	LOWER MIDDLE	MARRIED	BOOKED	16/7/21	23/4/22	35WKS1DAY	G1	S
131	TK	27	GK	1366173	SECONDARY	HOUSEWIFE	2	LOWER MIDDLE	MARRIED	BOOKED	20/9/21	27/6/22	34WKS2DAY	G1	S
132	C	34	JS	1360587	SECONDARY	HOUSEWIFE	6	LOWER MIDDLE	MARRIED	BOOKED	19/11/21	26/9/22	36WKS	G3P1L0	S
133	K	32	KK	1363612	SECONDARY	PVT JOB	7	UPPER MIDDLE CLASS	MARRIED	BOOKED	17/11/21	24/9/22	36WKS	G1	S
134	RB	30	JK	1289340	PRIMARY	HOUSEWIFE	7	LOWER MIDDLE	MARRIED	BOOKED	30/12/21	10-07-2022	34WKS	G1	S
135	NG	24	MG	1389456	SECONDARY	HOUSEWIFE	2	LOWER MIDDLE	MARRIED	BOOKED	22/12/21	10-03-2022	33WKS2DAYS	G2P1L1	S
136	SK	28	gk	1298450	SECONDARY	PVT JOB	1	UPPER CLASS	MARRIED	BOOKED	01-01-2022	7/10/22	34WKS	G2P1L1	S
137	NG	30	MG	1360884	SECONDARY	HOUSEWIFE	2	LOWER MIDDLE	MARRIED	BOOKED	31/12/21	7/10/22	33WKS6DAYS	G1	A

2	CLEAR	NO	B	MULTI	120/80	86	NORMAL	LINEA NIGRA+,STRIA+,TRANSVERSE	34-36	LONG	CEPHALIC	NORMAL	136	-
72	CLEAR	NO	B	MULTI	110/70	78	NORMAL	LINEA NIGRA+,STRIA+	32-34	LONG	CEPHALIC	NORMAL	128	-
3	CLEAR	NO	B	PRIMI	110/80	86	NORMAL	LINEA NIGRA+,STRIA+	30-32	LONG	CEPHALIC	NORMAL	156	-
3	CLEAR	NO	B	PRIMI	110/70	76	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	146	-
24	CLEAR	NO	B	MULTI	120/80	90	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	156	-
4	CLEAR	NO	B	PRIMI	110/70	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	158	-
2	CLEAR	NO	B	MULTI	120/80	90	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	148	-
1	CLEAR	NO	B	PRIMI	110/70	102	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	145	-
2	CLEAR	NO	B	MULTI	120/70	100	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	156	-
2	CLEAR	NO	B	PRIMI	110/70	99	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	145	-
4	CLEAR	NO	B	MULTI	120/80	88	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	165	-
1	CLEAR	NO	B	PRIMI	110/70	98	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	154	-
12	CLEAR	NO	B	MULTI	120/80	76	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	146	-
4	CLEAR	NO	B	PRIMI	160/90	88	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	153	-
3	CLEAR	NO	B	MULTI	140/70	82	NORMAL	LINEA NIGRA+,STRIA+	32-34	LONG	CEPHALIC	NORMAL	145	-
3	CLEAR	NO	B	MULTI	120/80	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	159	-
3	CLEAR	NO	B	MULTI	110/70	78	NORMAL	LINEA NIGRA+,STRIA+	28-30	LONG	BREECH	NORMAL	126	-
3	CLEAR	NO	B	MULTI	110/80	90	NORMAL	LINEA NIGRA+,STRIA+,VERTICAL SCAR +	34-36	LONG	CEPHALIC	NORMAL	148	-
4	CLEAR	NO	B	MULTI	120/70	84	NORMAL	LINEA NIGRA+,STRIA+,TRANSVERSE SCAR+	34-36	LONG	CEPHALIC	NORMAL	138	-
72	CLEAR	NO	B	MULTI	110/70	78	NORMAL	LINEA NIGRA+,STRIA+,TRANSVERSE SCAR+	34-36	LONG	CEPHALIC	NORMAL	132	-
4	CLEAR	NO	B	MULTI	120/70	82	NORMAL	LINEA NIGRA+,STRIA+	30-32	LONG	CEPHALIC	NORMAL	146	-
24	CLEAR	NO	B	PRIMI	110/70	86	NORMAL	LINEA NIGRA+,STRIA+	28-30	LONG	BREECH	DECREASED	156	-
24	CLEAR	NO	B	PRIMI	120/86	98	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	146	-
72	CLEAR	NO	B	MULTI	110/80	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	DECREASED	136	-
36	CLEAR	NO	B	PRIMI	110/81	86	NORMAL	LINEA NIGRA+,STRIA+	32-34	LONG	CEPHALIC	NORMAL	123	-
72	CLEAR	NO	B	MULTI	110/82	57	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	126	-
48	CLEAR	NO	B	MULTI	110/83	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	136	-
72	CLEAR	NO	B	MULTI	110/84	84	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	145	-
24	CLEAR	NO	B	PRIMI	110/85	76	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	135	-
36	CLEAR	NO	B	PRIMI	110/86	72	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	154	-
3	CLEAR	NO	B	MULTI	110/87	100	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	146	-
2	CLEAR	NO	B	PRIMI	110/88	102	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	152	-
12	CLEAR	NO	B	PRIMI	110/89	94	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	136	-
6	CLEAR	NO	B	MULTI	110/90	92	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	148	-
2	CLEAR	NO	B	MULTI	110/91	90	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	146	-
NA	CLEAR	NO	C	PRIMI	110/70	68	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	160	-

D	-	12	8	180	15	2	0.3	-	GROWTH -
D	-	10	8	150	16	2	0.1	-	GROWTH -
D	-	12	5	190	14	2	0.1	-	GROWTH -
D	-	12	8	200	7	1	0.1	-	GROWTH -
D	-	10	9	160	17	3	0.1	-	GROWTH -
D	-	12	7	200	15	3	0.1	-	GROWTH -
D	-	13	5	160	16	2	0.2	-	GROWTH -
D	-	8	4	148	14	3	0.1	-	GROWTH -
D	-	9	8	367	15	2	0.2	-	GROWTH -
D	-	8.9	4	238	16	3	0.1	-	GROWTH -
D	-	6.8	3	450	7	2	0.2	-	GROWTH -
D	-	9	9	160	16	1	0.3	-	GROWTH +
D	-	12	10	158	14	2	0.1	-	GROWTH -
D	-	10	14	160	15	3	0.1	-	GROWTH -
D	-	12	10	190	16	1	0.2	-	GROWTH -
D	-	9.9	13	200	14	3	0.2	-	GROWTH -
D	-	10	17	190	12	2	0.2	-	GROWTH -
D	-	12	6	190	12	2	0.1	-	GROWTH -
D	-	10	7	150	12	2	0.1	-	GROWTH -
D	-	9	5	180	7	1	0.1	-	GROWTH -
D	-	12	10	146	12	1	0.2	-	GROWTH -
D	-	12	19	130	14	2	0.1	-	GROWTH -
D	-	14	8	170	12	2	0.1	-	GROWTH -
D	-	13	7	150	14	2	0.3	-	GROWTH -
D	-	8	6	130	7	3	0.02	-	GROWTH -
D	-	8.5	4	160	7	3	0.01	-	GROWTH -
D	-	6	9	140	7	0	0.01	-	GROWTH -
D	-	9	10	158	15	3	0.02	-	GROWTH -
D	-	9.6	4	169	16	3	0.02	-	GROWTH -
D	-	9.2	5	225	14	0	0.01	-	GROWTH -
D	-	8.7	13	158	18	3	0.02	-	GROWTH +
D	-	9	6	190	17	2	0.01	-	GROWTH -
D	-	7.8	15	168	13	0	0.01	-	GROWTH -
D	-	10	9	169	16	1	0.2	-	GROWTH -
D	-	13	5	200	14	2	0.2	-	GROWTH -
D	-	12	4	234	16	0.5	0.2	-	GROWTH -

138	s	40	ks	1362819	GRADUATE	HOUSEWIFE	3	UPPER MIDDLE CLASS	MARRIED	BOOKED	19/11/21	26/8/22	36WKS	G2A1	A
139	AG	30	MS	1359705	GRADUATE	PVT JOB	5	LOWER MIDDLE	MARRIED	BOOKED	11/12/21	18/9/22	34WKS	G2P1L1	A
140	PK	22	JB	1361367	GRADUATE	PVT JOB	4	UPPER ClASS	MARRIED	BOOKED	25/12/21	1/10/22	35WKS	G1	A
141	JK	29	YS	456734	SECONDARY	PVT JOB	6	UPPER MIDDLE CLASS	MARRIED	BOOKED	7/12/21	15/9/22	35WKS 4DAYS	G3A2	A
142	S	29	KS	1293788	GRADUATE	PVT JOB	12	UPPER MIDDLE CLASS	MARRIED	BOOKED	7/12/21	13/9/22	36WKS2DAYS	G1	A
143	P	38	JS	1361545	GRADUATE	GOVT JOB	10	UPPER MIDDLE CLASS	MARRIED	UNBOOKED	24/12/21	1/10/22	34WKS	G1	A
144	G	24	LL	1261467	SECONDARY	PVT JOB	4	UPPER MIDDLE CLASS	MARRIED	BOOKED	27/12/21	3/10/22	34WKS	G2A1	A
145	D	26	KJ	1362852	SECONDARY	HOUSEWIFE	3	LOWER CLASS	MARRIED	BOOKED	21/12/21	28/9/2022	35WKS 6DAYS	G2P1L0	A
146	J	34	TS	1331765	PRIMARY	HOUSEWIFE	5	LOWER MIDDLE	MARRIED	BOOKED	17/12/21	24/9/22	36WKS	G1	A
147	P	30	KK	1143456	GRADUATE	HOUSEWIFE	6	UPPER LOWER CLASS	MARRIED	BOOKED	20/12/21	26/9/22	34WKS5DAYS	G1	A
148	p	28	AA	1260779	GRADUATE	GOVT JOB	4	UPPER CLASS	MARRIED	BOOKED	26/12/21	10-02-2022	36WKS	G2P1L1	A
149	N	40	VK	1239051	SECONDARY	PVT JOB	5	UPPER CLASS	MARRIED	BOOKED	22/6/21	29/3/22	36WKS	G1	A
150	G	32	K	536742	GRADUATE	GOVT JOB	6	UPPERCLASS	MARRIED	BOOKED	07-09-2021	16/4/22	35WKS	G2P1L1	A

NA	CLEAR	NO	C	MULTI	120/70	76	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	158	-
NA	CLEAR	NO	C	MULTI	110/70	82	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	146	-
NA	CLEAR	NO	C	PRIMI	120/70	80	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	146	-
NA	CLEAR	NO	C	MULTI	110/70	82	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	BREECH	NORMAL	152	-
NA	CLEAR	NO	C	PRIMI	110/80	80	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	142	-
NA	CLEAR	NO	C	PRIMI	120/70	82	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	126	-
NA	CLEAR	NO	C	MULTI	110/70	80	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	148	-
NA	CLEAR	NO	C	MULTI	120/70	82	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	156	-
NA	CLEAR	NO	C	PRIMI	130/70	90	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	145	-
NA	CLEAR	NO	C	PRIMI	140/70	86	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	146	-
NA	CLEAR	NO	C	MULTI	150/80	82	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	160	-
NA	CLEAR	NO	C	PRIMI	130/90	80	NORMAL	LINEA NIGRA+,STRIA+	34-36	LONG	CEPHALIC	NORMAL	145	-
NA	CLEAR	NO	C	MULTI	140/70	86	NORMAL	LINEA NIGRA+,STRIA +	34-36	LONG	CEPHALIC	NORMAL	120	-

D	-	9.7	8	245	17	1	0.1	-	GROWTH +
D	-	9.9	9	150	18	1	0.1	-	GROWTH -
D	-	7.7	16	190	15	0.3	0.1	-	GROWTH -
D	-	8	16	168	16	1	0.2	-	GROWTH -
D	-	9.8	20	200	14	1	0.1	-	GROWTH -
D	-	9.6	12	345	18	1	0.2	-	GROWTH -
D	-	9.5	10	120	14	1	0.1	-	GROWTH -
D	-	8	10	138	14	0.6	0.1	-	GROWTH -
D	-	8.6	11	167	14	0.6	0.2	-	GROWTH -
D	-	9.5	13	230	15	1	0.2	-	GROWTH -
D	-	9	15	167	12	1	0.2	-	GROWTH -
D	-	13	13	159	15	0.01	0.1	-	GROWTH -
D	-	12	10	160	17	0	0.1	-	GROWTH +

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Date 25/01/22

The Principal,
DMC, Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.10.2021 has approved the plan of thesis of **Heena**, a student of your college for **MD Obstetrics & Gynaecology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Estimation of urea and creatnine in vaginal fluid in preterm pre-labour rupture of membranes.

Supervisor
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The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

73. *If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.*
74. *The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.*

ESTIMATION OF UREA AND CREATNINE IN VAGINAL FLUID IN PRETERM PRE-LABOUR RUPTURE OF MEMBRANES

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN

PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

OBSTETRICS & GYNAECOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

MARCH, 2021

DR HEENA

DEPARTMENT OF OBSTETRICS & GYNAECOLOGY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	ESTIMATION OF UREA AND CREATNINE IN VAGINAL FLUID IN PRETERM PRE-LABOUR RUPTURE OF MEMBRANES
For the degree of	MD (Obstetrics &Gynaecology)
Name of the candidate	DrHeena
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Co-supervisor(s)	Dr. Navjot Kaur Bajwa, Professor & Head, Department of Biochemistery, DMCH, Ludhiana Dr. Shweta Gupta, Professor, Department of Obstetrics & Gynaecology, DMCH, Ludhiana
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Preterm Pre-labour rupture of membrane is associated with an increased maternal and perinatal morbidity and mortality. So confirmatory diagnosis is essential before initiating the definitive treatment of Preterm Pre-labour rupture of membrane.

Aim of Study: To determine the diagnostic accuracy of vaginal washing fluid urea and creatinine levels in the detection Preterm Pre-labour rupture of membrane. To give suitable recommendations based on the study findings.

Materials & Methods: This will be a prospective case control study. Women having gestational age of 28 to 37weeks Will be divided into three equal groups: GROUP[A] 50 pregnant women with history of leaking per vagina and confirmed leak on per speculum examination (case group), GROUP[B] (suspect)50 pregnant women with suspected history of leaking and not confirmed on P/S examination. GROUP[C] 50 pregnant women with no leaking per vaginum (control group) will be recruited. Data analysis will be done by ANOVA and chi square test.

Clinical Significance: Measurement of vaginal fluid urea and creatinine concentration is easy, cost effective and can be performed without much technical assistance

Keywords: Preterm Pre-labour Rupture of Membranes (PPROM); Urea; Creatinine; Vaginal Discharge

(Signature) Candidate	(Signature) Co-supervisor	(Signature) Co-supervisor	(Signature) Supervisor	(Signature) Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"ESTIMATION OF UREA AND CREATNINE IN VAGINAL FLUID IN PRETERM PRE-LABOUR RUPTURE OF MEMBRANES"** exist in the Department of Obstetrics and Gynaecology, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate herself under our supervision and guidance.

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Approved: Yes / No

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Chairperson
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Approved: Yes / ~~No~~

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4	DATE OF ADMISSION OF COURSE	30/JUNE/2020
5	TITLE OF THE TOPIC	ESTIMATION OF UREA AND CREATNINE IN VAGINAL FLUID IN PRETERM PRE-LABOUR RUPTURE OF MEMBRANES

6. BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Preterm birth is one of the important maternal health issue. Its incidence is increasing in developed and developing countries and it remains the most important determinant of adverse fetal outcome.[1]

When the membrane ruptures spontaneously before the onset of labour, it is called pre labour rupture of membrane.[PROM][1] when rupture occurs before 37 completed weeks it is called pre term pre-labour rupture of membranesi PPROM.[1]

The incidence of term prelabour rupture is about 10% and that of preterm pre labour rupture of membrane is 3% globally.[1] Usually labour sets in within 12 to 24 hours after rupture of membrane.[1]Spontaneous onset of labour in term PROM is 86% and in PPROM is around 40%.[1]

Accurate history, clinical examination and specialized tests are the hallmark for diagnosing Preterm prelabour rupture of membranes. Failure to identify patient or false positive diagnosis of Preterm prelabour rupture of membranes may lead to inappropriate management and serious maternal and neonatal complications or unnecessary obstetric interventions. [2]

Inability to diagnose Preterm prelabour rupture of membranes in time can lead to obstetric complications like cord prolapse, abruption, chorioamniotis, postpartum endometritis, neonatal sepsis/respiratory distress syndrome, Necrotizing Enterocolitis, Interventricular hemorrhage dry labour ,fetal pulmonary hypoplasias.

The three conventional findings made by the clinician which are considered gold standard in the diagnosis of Preterm prelabour rupture of membranes [3];

1) Observation of clear amniotic fluid flow or accumulation of fluid at posterior fornix with a sterile speculum.

2) Observation of transition from yellow to blue with pH indicator paper due to basic amniotic fluid flow (nitrazine test)

3) Detection of palm leaf-pattern in dried amniotic fluid with microscopic method (fern test).

However these conventional methods are associated with drawbacks. History is reliable in 10% to 50% of cases speculum examination of fluid leakage from the cervix was associated with 12% - 30% false negative results.[4]

Nitrazine test was associated with false positive or negative results due to contamination by urine, blood or meconium, antibiotics, vaginal and cervical infections. [4]

Fern test was also associated with 13-30% false negative and 5-30% false positive results [4].

Even amniotic fluid determination by ultrasound examination was not a reliable test to evaluate membrane rupture because it cannot differentiate Preterm Pre-labour Rupture of Membrane from other causes of oligohydramnios[5]

Intra amniotic dye injection and observation for fluid passage transvaginally was designated an “unequivocal” diagnostic method for confirmation of membrane rupture, but this invasive test carries increased maternal and fetal risk [6].

The Amnisure rupture of membranes test is another new test that is easy, fast, and minimally invasive, with high sensitivity and specificity [7,8]. However, Amnisure is not available in many centers and it is expensive also.

Many biochemical diagnostic modalities for Preterm Pre-labour Rupture of Membrane have been described, like measurement of vaginal PH, alpha fetoprotein (AFP), insulin growth factor binding protein-1(IGFBP-1), fetal fibronectin tests, human chorionic gonadotropin (HCG), prolactin, urea, creatinine.[4,5, 9-13].

The rationale of these markers stems from their high concentrations in amniotic fluid compared with normal vaginal secretions. These tests are based on the identification in the vaginal washing of one or more of these biochemical markers that are present in the setting Preterm prelabour rupture of membranes but absent in women with intact membranes. However, despite the improved diagnostic potential of

these markers, they have not become popular due to their complexity and high cost.[9]

Recently, the focus has been on urea and creatinine in cervicovaginal discharge. Measurement of urea and creatinine in the vaginal fluid for the diagnosis of Preterm prelabour rupture of membranes is based on the concept that fetal urine is the prime component of amniotic fluid in the second half of pregnancy. The fetus starts excreting urine into the amniotic fluid at 8th to 11th week of gestation. As there is no need for extra equipment and reagent, introduction of this method into routine use is feasible and practical. So, the present study is designed to evaluate the reliability of vaginal washing fluid urea and creatinine for diagnosis of Preterm prelabour rupture of membranes and to determine the cut off value for urea and creatinine in vaginal washing fluid.

6.2 REVIEW OF LITERATURE

Amniotic fluid surrounds the embryo and fetus during development and has a multiple functions. Physically, it protects the fetus trauma. Furthermore, it protects the umbilical cord by providing a cushion between the fetus and the umbilical cord thus reducing risk of compression between the fetus and the uterine wall.[14] Amniotic fluid also helps protect the fetus from infectious agents, due to its inherent antibacterial properties. Additionally, it serves as a reservoir of fluid and nutrients for the fetus containing: proteins, electrolytes, immunoglobulins, and vitamins from the mother. It provides the necessary fluid, space, and growth factors to allow normal development and growth of fetal organs such as the musculoskeletal system, gastrointestinal system, and the pulmonary system.[15]. The amniotic fluid volumes in normal pregnancy exhibit a wide variation; the volume increases progressively 30ml at 10weeks, 300mls at 20weeks, 600mls at 30weeks, and 1000mls at 38weeks. From term there is a rapid fall in volume 800mls at 40weeks and 350mls at 42 weeks. The reason for the late reduction has not been explained. The fluid is initially secreted by the amnion, but by the 10th week it is mainly a transudate of the foetal serum via the skin and the umbilical cord. From 16 weeks gestation, the foetal skin becomes impermeable to water and the net increase in amniotic fluid is through a small imbalance between contributions of fluid through the kidneys and lung fluids and removal by foetal swallowing.[16]

Amniotic fluid, maternal blood and urine contain urea and creatinine. Pregnant women in the first half of pregnancy have a mean creatinine concentration of 0.6mg/dl in the amniotic fluid which is similar to maternal serum [17,18]. Gradual increase of creatinine concentration is noticed in amniotic fluid between 20 and 32 weeks of gestation, which rises even more rapidly to reach a value as high as two to four times that of maternal serum [17,18]

A creatinine concentration of 1.75mg/dl or more correlates significantly with a gestational age of 37 weeks or more [18].Therefore, it can be summrised that vaginal urea and creatinine can be used not only in the

diagnosis of Preterm prelabour rupture of membranes but also for fetal maturation test in case of preterm labor. Reliability of conventional test does not match with the patient's leaking history, so the search for simple, fast, easily accessible and non-invasive diagnostic methods to detect rupture of membranes is still in demand. This study considers testing the diagnostic accuracy of urea and creatinine in vaginal fluid, which can be easily accessible in low resource community settings for Preterm prelabour rupture of membranes

Kafali et al. [2007] were first to use urea for diagnosis of Preterm prelabour rupture of membranes. In their study, the sensitivity, specificity, Negative and positive predictive value were all 100% in detecting Preterm prelabour rupture of membranes by evaluation of vaginal fluid urea and creatinine concentration with cut off values of 12 and 0.6mg/dl respectively [18]. Mohamed et al. had also found 100% sensitivity, specificity, Negative Predictive value and Positive Predictive Value of evaluation with cut off of urea 13.2 mg/dl and creatinine 0.31mg/dl in detecting Preterm prelabour rupture of membranes [19].

Zanjani et al. [2012] studied the reliability of vaginal fluid creatinine for the diagnosis of premature rupture of membranes. The creatinine level was significantly higher in the confirmed group than in the other two groups ($P < 0.0010$). They found 96.7% sensitivity, 100% specificity, 100% Positive Predictive Value, 96.8% Negative Predictive value with optimal cutoff value of 0.5mg/dl. They concluded that it is a valid and simple test, especially considering that it costs much less than hospitalization or other tests [2].

Kariman et al. [2013] also studied 2 groups to compare vaginal fluid urea and creatinine in confirmed cases and normal controls. They found the mean level of vaginal fluid urea and creatinine in the Preterm prelabour rupture of membranes group to be significantly higher than in the control group.[20]

Osman et al. [2014] studied 3 groups, and compared AFI and vaginal fluid urea, creatinine and β-hCG. They showed a statistically significant difference among all groups regarding AFI, urea, creatinine and β-hCG levels. They found sensitivity, specificity, Positive Predictive Value,

Negative Predictive value and accuracy of urea and creatinine were all 100% with a cut off value of > 0.41 mg/dl and > 0.23 mg/dl. They concluded urea and creatinine in vaginal washings can be accurately used in diagnosing suspected Preterm prelabour rupture of membranes and are more accurate than β-hCG[21].

Tigga et al. [2015] studied 2 groups, and compared vaginal fluid alpha fetoprotein, prolactin creatinine and β-hCG. They found that all the four markers were significantly higher in the patients with Preterm prelabour rupture of membranes in comparison to those without Preterm prelabour rupture of membranes. They found sensitivity, specificity, Positive Predictive value, Negative Predictive value and efficiency of creatinine were 100%, 92%, 92.59% , 100% and 96% efficiency with a cut off value of 0.1641 mg/dl and Creatinine was reported to be simple, cheap, reliable and easily available method for diagnosing Preterm Pre-labour Rupture of Membrane [12]

Ghasemi et al. [2016] studied in 2 groups, 80 confirmed Preterm Pre-labour Rupture of Membrane patients and 80 controls and compared vaginal fluid prolactin, β-hCG, urea, and creatinine. They also showed that all the four markers were significantly higher in the patients with Preterm prelabour rupture of membranes in comparison to those without Preterm Pre-labour Rupture of Membrane ($p < 0.001$) .An optimal cutoff level of 3.5 mg/dl for urea and 0.25 mg/dl for creatinine was seen in their study. The sensitivity, specificity, positive and negative predictive values to diagnose Preterm Pre-labour Rupture of Membrane were calculated and found to be as 79.7%, 82.5%, 81.8% and 80.4% for urea and 74.6%, 85%, 83% and 77.2% for creatinine. They reported less diagnostic value of urea and creatinine for detecting Preterm prelabour rupture of membranes because of the difference in laboratory method analysis and cut off points [13].

Gezer et al. [2017] conducted a study an optimal cutoff level of 6.7 mg/dl for urea and 0.12 mg/dl for creatinine in vaginal fluid. They finally came up with a suggestion that urea levels > 6.7 mg/dl and creatinine levels> 0.12 mg/dl in vaginal fluid, to diagnose Preterm Pre-labour Rupture of Membrane in approximately 88% and 89% of women

respectively, if seen between 24 and 37 weeks. They also hinted that in patients with shorter delivery interval, raised vaginal urea and creatinine levels may suggest a large defect in amniotic membrane or increased production by fetus.[22]

Although the exact aetiology of pre-labour rupture of membranes is poorly understood, several maternal risk factors have been implicated in its aetiology. These include the previous history of PROM, bacterial vaginosis, cervical incompetence, uterine over-distension, prior cervical surgery (eg: conization), poor nutrition and poor socio-economic status, connective tissue disorders e.g. Ehler's-Danlos Syndrome among others.

6.3 AIMS AND OBJECTIVES OF THE STUDY

- To determine the diagnostic accuracy of vaginal washing fluid urea and creatinine levels in the detection of Preterm Pre-labour Rupture of Membrane
- To give suitable recommendations based on the study findings.

7. MATERIALS AND METHODS

7.1 Source of Data

This will be a prospective case-control study performed in the Department of Obstetrics and Gynaecology in collaboration with the Department of Biochemistry at Dayanand Medical College and Hospital, Ludhiana which is a tertiary care hospital.

An informed consent in the patients own language will be taken from all pregnant women who participated in the study. The sample size will be calculated based on accuracy level of diagnosis of Preterm Pre-labour Rupture of Membrane by the measurement of vaginal fluid urea and creatinine.

7.2 METHOD OF COLLECTION OF DATA

Pregnant women with singleton live fetus (without any abnormality) coming to the labour room and willing to participate in the study will be taken into our study. Gestational age of pregnancy of the women in our study will be in between 28 and 37 completed weeks. Total 150 women

- Group A- The Study (Cases) Group This group will consist of pregnant women with the history of leaking per vagina and to confirm leak on per speculum / per vaginal examination.
- Group B- Suspected leaking when the clinician is not sure
- Group C- (The Control Group) This group consisted of pregnant women who did not either had the history of leaking per vagina or leak on speculum examination.

Total no of cases will be 150 with 50 in each group with H/O leaking per vaginum coming to labour room.

METHOD:-The per-speculum examination will be done and presence or absence of pooling in the posterior fornix noted. Vaginal wash fluid collection will be done during per speculum examination. Five ml of sterile saline will be instilled into the posterior fornix and 3 ml of it aspirate out with the same syringe and send to the laboratory for centrifugation and estimation of urea and creatinine. The sample will be first centrifuged at 3000 rpm for 10 minutes and then processed.

Urea will be analysd by the Urease method

Creatinine by the Jaffe's alkaline Picrate method.

Tests will be performed in the Auto-analyser and values were noted for analysis.

Total 150 patients will be prospectively evaluated for inclusion in this study.

INCLUSION CRITERIA:

- Antenatal women with singleton pregnancy, gestational age between 28 – 37wks with confirmed leaking /suspected leaking with no labour pains.

EXCLUSION CRITERIA:

- Multiple pregnancies
- Congenital foetal anomaly
- History of vaginal infection
- Intrauterine foetal demise
- Meconium stained liquor
- women not willing to participate in the study.

STUDY SAMPLE: The study will be preformed on 150 pregnant women in labour ward with Preterm Pre-labour Rupture of Membrane. GP-A GP-B, GP-C, admitted for period of amenorrhea.

NUMBER OF CASES: 150 pregnant women with 50 in each group.

Outcome: Urea and creatinine in vaginal washing fluid is a reliable and less costly marker for detection of Preterm Pre-labour Rupture of Membrane.

STATISTICAL ANALYSIS: Data will be described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. Comparison of quantitative variables between the study groups would be done using ANOVA.

For comparing categorical data, Chi square ($\chi 2$) test will be performed and exact test was used when the expected frequency is less than 5.

A probability value (p value) less than 0.05 will be consider statistically significant. All statistical calculations will be done using (Statistical

Package for the Social Science) SPSS 21version (SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

Yes vaginal fluid wash will be collected for estimation of urea and creatinine

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

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PROFORMA

Sr. No

NAME AGE

HUSBAND NAME DATE OF ADMISSION

MRD NO. PHONE NO.

RESIDENTIAL ADDRESS

EDUCATION OCCUPATION

MARRIED SINCE SOCIOECONOMIC STATUS

RELATIONSHIP STATUS

BOOKED /UNBOOKED

MENSTURAL HISTORY-LMP EDOD POG

OBSTETRICS FORMULA

CHIEF COMPLAINT:-LEAKING -present /suspect /absent

Duration colour amount

Labour pains

DIAGNOSIS: group- A group –B GROUP -C

OBSTETRICS HISTORY

GENRAL EXAMINATION

BP PULSE TEMP

Signature of Candidate **Signature of Supervisor**

INSPECTION

PER ABDOMEN

FH

SFH

AG

Fetal lie

Presentation

Amniotic fluid

AUSCULTATION

LOCAL EXAMINATION

VULVAL PAD

PER SPECULUM

INVESTIGATION

HB PLT TLC

HVS VAGINAL FLUID SAMPLING

USG FWB

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o, S/o.....
.....am willing to participate in the study **"ESTIMATION OF UREA AND CREATNINE IN VAGINAL FLUID IN PRETERM PRE-LABOUR RUPTURE OF MEMBRANES"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

....
Signature of the Witness. Signature of the patient

Name:

Signature of Candidate **Signature of Supervisor**

मरीज अनुमति फार्म

तिथि _____

मैं _____ पत्नी/पुत्र/पुत्री _____
निवासी _____

इस शोधकार्य **"ESTIMATION OF UREA AND CREATNINE IN VAGINAL FLUID IN PRETERM PRE-LABOUR RUPTURE OF MEMBRANES"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

_____ _____

गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

_____

अन्वेषक के हस्ताक्षर

_____

विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____

ਵਾਸੀ _____

"ESTIMATION OF UREA AND CREATNINE IN VAGINAL FLUID IN PRETERM PRE-LABOUR RUPTURE OF MEMBRANES" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

_____ _____

ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

_____

ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

PJK1

_____

ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ